A COMPARATIVE EVALUATION OF BUPIVACAINE WITH NALBUPHINE VERSUS BUPIVACAINE WITH TRAMADOL FOR POST OPERATIVE ANALGESIA IN ELECTIVE LOWER LIMB REVASCULARIZATION SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA

A Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the requirements

for the award of the degree

M.D. (BRANCH-X)
ANAESTHESIOLOGY

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE
MADRAS MEDICAL COLLEGE
CHENNAI, TAMILNADU

APRIL 2017

CERTIFICATE

This is to certify that the dissertation titled **"A COMPARATIVE EVALUATION OF BUPIVACAINE WITH NALBUPHINE VERSUS BUPIVACAINE WITH TRAMADOL FOR POST OPERATIVE ANALGESIA IN ELECTIVE LOWER LIMB REVASCULARIZATION SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA"** presented herein by **Dr. SUGANYA. B** is an original work done in the Institute of Anaesthesiology and Critical care , Madras Medical College, Chennai for the partial fulfilment of the regulations of the Tamilnadu Dr. M.G.R. Medical University for the award of degree of M.D. (Anaesthesiology) Branch X during the academic period 2014-2017.

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This is to certify that the dissertation titled **"A COMPARATIVE EVALUATION OF BUPIVACAINE WITH NALBUPHINE VERSUS BUPIVACAINE WITH TRAMADOL FOR POST OPERATIVE ANALGESIA IN ELECTIVE LOWER LIMB REVASCULARIZATION SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA"** is a genuine work done by **Dr. SUGANYA. B** under my supervision and guidance in the Institute of Anaesthesiology and Critical Care , Madras Medical College, Chennai for the partial fulfilment of the requirements for M.D. (Anaesthesiology) Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in April 2017.

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DECLARATION BY THE CANDIDATE

I, **Dr. SUGANYA. B,** solemnly declare that the dissertation, titled **"A COMPARATIVE EVALUATION OF BUPIVACAINE WITH NALBUPHINE VERSUS BUPIVACAINE WITH TRAMADOL FOR POST OPERATIVE ANALGESIA IN ELECTIVE LOWER LIMB REVASCULARIZATION SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA"**, is a bonafide work done by me during the academic period of March 2014 to August 2017 at Madras Medical College and Hospital, Chennai under the expert supervision of **Dr. N. LATHA, M.D., D.A.,** Professor and Head of the Department, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai. This thesis is submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the rules and regulations for the M.D. degree examinations in Anaesthesiology to be held in April 2017.

I have not submitted this dissertation to any other University for the award of degree or diploma

Dr. SUGANYA.B

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ACKNOWLEDGEMENT

I wish to express my sincere thanks to **Prof. Dr.MURALIDHARAN., MS,Mch** Dean, Madras Medical College for having permitted me to utilize the facilities of the hospital for the conduct of the study.

I thank **Prof. Dr.B.KALA.M.D., D.A,** Professor and Head, Institute of Anaesthesiology and Critical Care, Madras Medical College for her constant encouragement and support.

My heartfelt gratitude to **Prof. LATHA.N, M.D., D.A.,** Professor, Institute of Anaesthesiology and Critical Care, Madras Medical College for her motivation, valuable suggestions, expert supervision, guidance and for making all necessary arrangements for conducting this study.

I thank **Prof. Dr. AMALOPAVLONATHAN, MS,Mch Professor and HOD (vascular surgery),** for his constant support and encouragement.

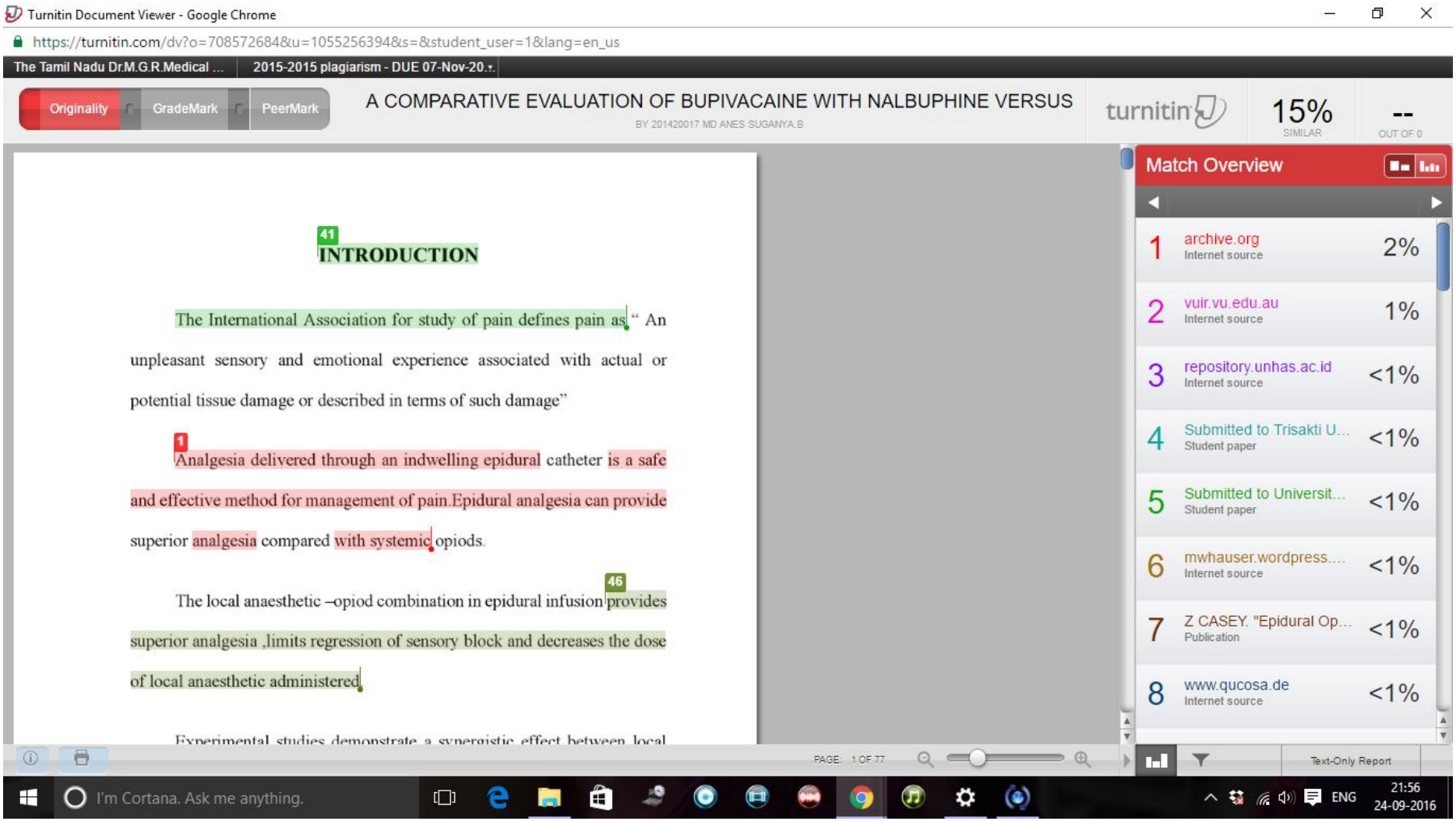
I express my heartfelt gratitude to my Assistant Professors **DR.CAROLIN VON MULLAI, M.D.,D.A., DR.BHUVANA, M.D. AND DR.ASHOK KUMAR ,M.D** who had evinced constant and keen interest in the progress of my study right from the inception till the very end and were instrumental in the successful completion of the study.

I wish to thank all my Professors and Assistant Professors especially for their aid and encouragement during the study.

My sincere thanks to all those post graduates who helped me during this study period.

I thank the staff nurses and theatre personnel, Madras Medical College for their cooperation and assistance.

I owe my gratitude to all the patients included in the study and their relatives, for their whole hearted co-operation and consent.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Experimental studies demonstrate a synergistic effect between local
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INTRODUCTION

CONTENTS

INTRODUCTION

The International Association for study of pain defines pain as " An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"

Analgesia delivered through an indwelling epidural catheter is a safe and effective method for management of pain.Epidural analgesia can provide superior analgesia compared with systemic opiods.

The local anaesthetic –opiod combination in epidural infusion provides superior analgesia ,limits regression of sensory block and decreases the dose of local anaesthetic administered.

Experimental studies demonstrate a synergistic effect between local anaesthetics and opiods,however clinical trials suggest an additive effect.

Nalbuphine (a synthetic opioid agonist-antagonist) and tramadol (a synthetic opioid) have advantages because of their rapid onset of action. These drugs being preservative free makes epidural administration possible.

AIM OF STUDY

To Compare Bupivacaine with Nalbuphine versus Bupivacaine with Tramadol for post operative analgesia in Elective lower limb revascularisation surgeries under compared spinal epidural anaesthesia, with respect to,

1. Post operative Visual Analogue Scale for pain score.
2. Intra-operative and post operative hemodynamics

VASCULAR PAIN

The relief of vascular pain is commonly a hall mark of the success of the medical or surgical therapy of vascular disease.

Large and medium sized arteries have two types of innervation -afferent (sensory) nerves and autonomic (sympathetic) nerves. Pain is the primary sensation transmitted via nociceptive afferents in arteries and veins. Position, temperature, and other such sensations do not appear to be transmitted via the innervation of blood vessels. Nociceptive receptors are usually free nerve endings, and pain is transmitted in the small unmyelinated A delta and C nerve fibers. These afferent nerves cell bodies are located in the dorsal root ganglia and their axons enter the spinal cord through the dorsal roots. These axons synapse in the dorsal gray matter of the cord with second - order neurons. Most pain is transmitted in the crossed lateral spinothalamic tract up the cord to third - order neurons in the thalamus. The paleospino thalamic tract, including the periaqueductal gray region of Ihe brainstem, is relevant to more diffuse, longer lasting pain probably, neuropathic pain.

In large and Medium sized arteries, nociceptive receptors appear to be stimulated by direct trauma, (eg. an arteriography needle), stretch (balloon dilatation / Stent) or shear (as in arterial dissection).

Nociception in large and medium sized veins is due to pain receptors in the venous adventitia, which appears to respond primarily to stretch (as in venous distensions or engorgement due to downstream thrombosis or other obstruction).

As demonstrated in extensive neuroanatomic work by Pick [22], sympathetic and sensory fibers enter the arterial and venous adventitia to form an intrinsic neural network (adventitial pexus), mostly composed of sensory afferent. From these plexus bundles of nonmyelinated fibres (sympathetic) approach the media (Border plexus) and extensions of this network ramify within the media (muscular plexus).

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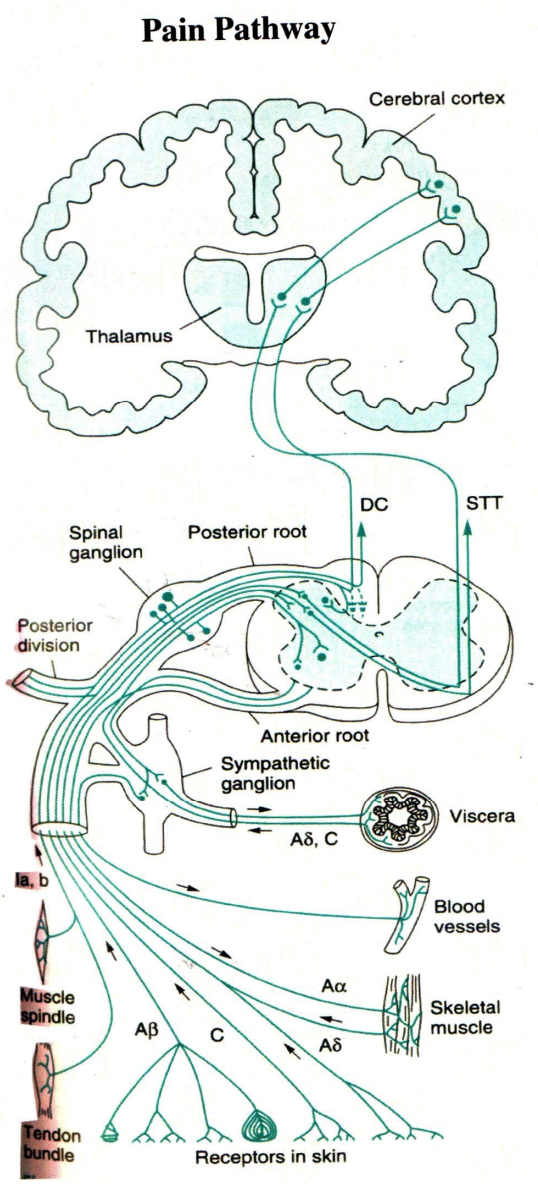


The basis for neuropathic pain, and how it is sustained, remains obscure. Such pain also appears to be transmitted by sensory afferents but unlike nociceptive pain, has autonomic (sympathetic nerve) components as well, resulting in the well - established (although poorly understood) role of sympathetic modulation for neuropathic pain by pharmacologic or anesthetic blockade or by sympathectomy.

Most nociceptive pain is relieved, according to teleologic definition by resolution of underlying noxious stimulus. The presence or severity of nociceptive pain warrants consideration of more invasive procedures to effect pain relief. Such procedures are characterized as neuroablative or neural augmentation. When used for management of pain, neuroablative procedures appear to be more effective, the more centrally they are performed - peripheral neurectomy, Rhizotomy, Dorsal Root Entry Zone, Cordotomy, Midbrain Tractotomy, Thalamotomy.

Sympathectomy is a unique form of neuroablative procedure that has an important role to play for various forms of sympathetically mediated or sympathetically sustained pain. Pain relief after sympathectomy results from following observations: Afferent fibres to extremities travel with sympathetic nerves; abnormal efferent activity in sympathetic nerve maintains pain and connections occur between - sympathetic somatic fibres.

According to Gorecki JP (1995) [9], the greatest importance in the management of pain is the use of intrathecal and epidural opiate narcotic. According to Krames E [16] (2002), Non - Narcotic agents such as local

anesthetics (Bupivacaine), GABA or somatostatin agonist, NMDA receptor agonists and calcium channel blockers may have a role to play in chronic intraspinal infusion modes.

The neurophysiology undergirding the use of epidural and intrathecal opiates is as follows: Modulation of afferent nociceptive input occurs in dorsal horn via several neurotransmitters. Receptors for various endogenous opioid systems (enkephalins and endorphins) regulate descending modulatory activity, usually in inhibitory fashion and multiple receptors for these substances are present in both central and peripheral nervous systems. Such receptors are the basis for favorable effects on pain of exogenously administered opioid analgesics.

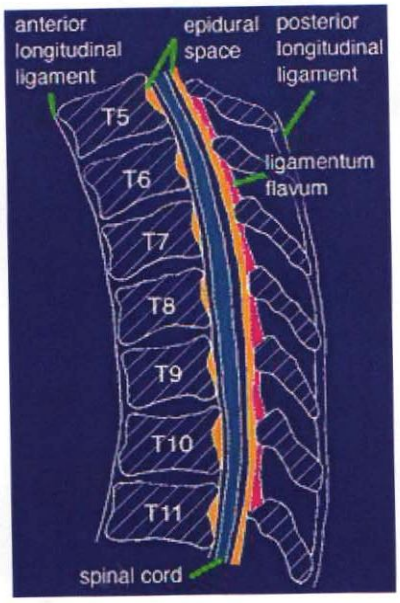
Rest pain, is characterized by a diffuse, ill localized aching or burning pain in distal foot, generally present initially when subject is recumbent or when leg and foot are elevated, symptoms dissipate if leg is hung over edge of bed or subject arises and limps around. The pathophysiology is likely that an ischemic neuropathy with positional malperfusion of small sensory nerves in distal foot. The symptoms of rest pain necessarily develop in most distal small arteries those farthest away from heart.

LERICHE – FONTAINE CLASSIFICATION			
STAGES	**SYMPTOMS**	**PATHO PHYSIOLOGY**	**PATHOPHYSIOLOGY CLASSIFICATIONS**
Stage I	Asymptomatic or effort pain	Relative hypoxia	Silent arteriopathy
Stage II A	Effort pain / pain-free waling distane >200m	Relative hypoxia	Stabilized arteriopathy, non-invalidant claudication
Stage II B	Pain-free walking distance <200m	Relative hypoxia	Instable arteriopathy, invalidant claudication
Stage III	Rest Pain	Cutaneos hypoxia, tissue acidosis, ischemic neuritis	Instable arteriopathy, invalidant claudication
Stage IV	Trophic lesion, necrosis or gangrene	Cutaneous hypoxia, tissue acidosis, necrosis	Evoluative arteriopathy

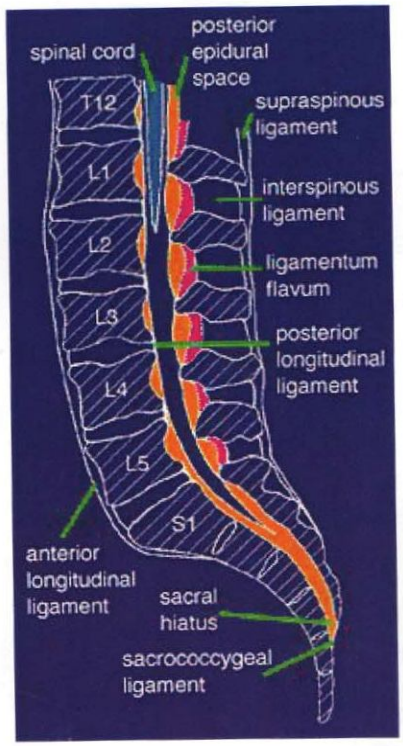
EPIDURAL ANATOMY

Epidural space is a potential space found between the outer periosteal lining of the spinal canal and inner spinal dural sac.

Boundaries of Epidural Space



Structures Pierced while entering Epidural Space



Boundaries

Above	:	Foramen magnum
Below	:	Sacro coccygeal membrane
In front	:	Posterior longitudinal ligament
Behind	:	Vertebral lamina and ligamentum flavum
Laterally	:	Pedicle and inter-vertebral foramina

Epidural space can be entered in the cervical, thoracic, lumbar and sacral region.

Structures pierced while entering epidural space

Median Approach

1) Skin
2) Subcutaneous Tissue
3) Interspinous ligament
4) Ligamentum Flavum

Paramedian Approach

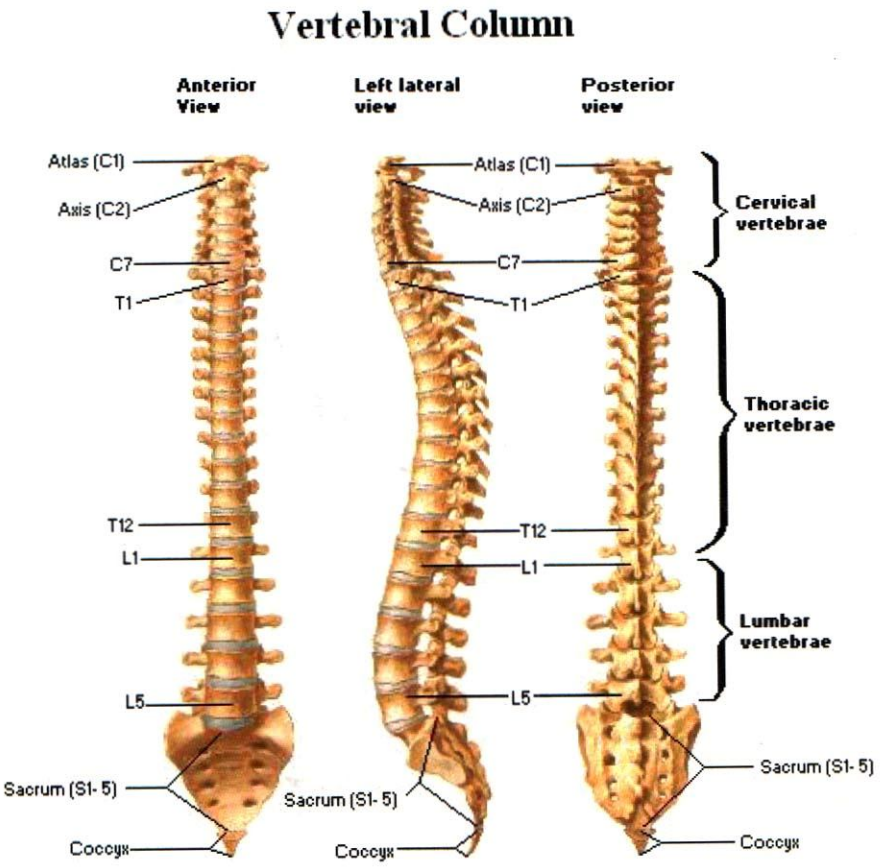
1) Skin
2) Subcutaneous Tissue
3) Ligamentum Flavum

Vertebral spine

L_1 to L_5 -90deg

T_7 to T_{12} -60 deg

T_2 to T_6 -30 to 40 deg



Ligamentum Flavum

It consists of tough elastic disposed in vertical direction connecting upper and lower borders of adjacent lamina, thickest in the lumbar region (3 to 5mm).

	Distance between flavum dura in mm	**Dural thickness in mm**
Cervical	1 to 1.5	2 to 1.5
Upper thoracic	2.5 to 3	1
Lower thoracic	4 to 5	1
Lumbar	5 to 6	0.66 to 0.33

Contents of Epidural space

1) Areolar tissue
2) Fat-pharmacological depot for LA
3) Lymphatics
4) Spinal arteries-Penetrating vessels of the spinal cord are end vessels, cord is vulnerable to ischemia.
5) Epidural veins-Valveless system connecting the pelvic veins to the occipital, basilar sinus, serves as alternate pathway for venous drainage from IVC to SVC

Nerve roots with dural sleeves

Dural sleeves cover the dorsal and ventral roots as they leave the subarachnoid space. They are covered by pampiniform plexus of veins. Plenty of blood vessels pierce the dura here. Arachnoid villi are also found at dural sleeves, more numerous in the lumbo-sacral region. The nerve roots are thicker in the cervical region and thinner in the lumbosacral region.

Meninges

Dura mater - Mechanical support.

Arachnoid matter -metabolically active

Pia mater

Epidural sieve at intervertebral foramina

There are 58 openings-50 laterally and 8 anteriorly. There are 2 grooves between atlas and occiput, 48 intervertebral foramina - 14 cervical, 24 thoracic, 10 lumbar and 8 sacral foramina. Local anesthetic solutions injected into epidural space will not only spread around dura within vertebral canal but also leave canal by these openings to enter paravertebral spaces. In young epidural sieve is soft, as age advances due to increasing condensation of the fibrous tissue it blocks the IV foramina restricting Local Anaesthetic to epidural space.

Covering of spinal nerve

They are the epineurium, perineurium and endoneurium. Epineurium and endoneurium are permeable, where as perineurium serves as a barrier to Local Anaesthetic.

Nerve fibres: They differ in function, size and anesthetic susceptibility

Type	**Diameter(microns)**	**Conduction Velocity(nVs)**	**Function**
A *a*	13 to22	70 to 120	Motor muscles, proprioception
Aβ	8 to 13	40 to 70	Joint afferent, pressure,
A γ	4 to 8	15 to 40	Touch Muscle spindle Efferent
A δ	1 to 4	5 to 15	Pain, heat, cold, pressure
B	1 to 3	3 to 14	Pre ganglionic, autonomic efferent
C	0.1 to 2.5	0.2 to 1.5	Pain, heat, cold, pressure

Type A and B fibres are myelinated and type C fibres are unmyelinated, so are most susceptible to Local Anaesthetics.

Epidural space is divided into posterior, anterior, and lateral compartments, which are connected to each other.

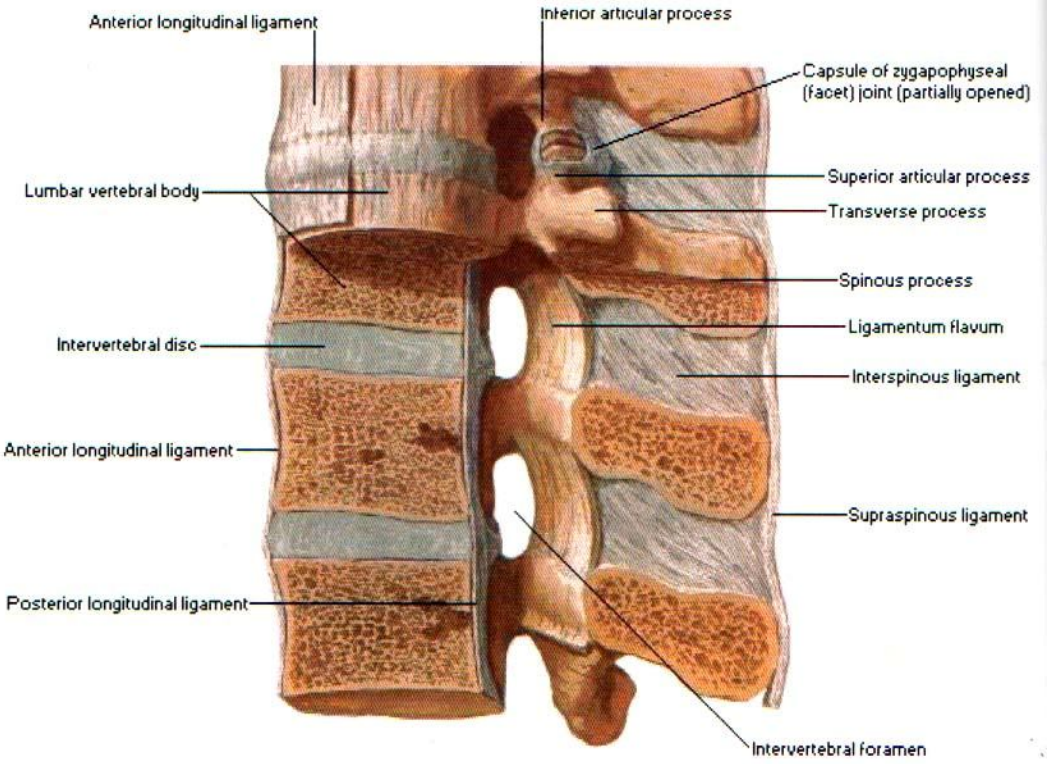
Posterior epidural space

In lumbar region in adults it is segmented and discontinuous. In thoracic region it is more continuous containing a thin layer of epidural fat. In cervico thoracic region epidural fat disappears and the dura contacts lamina directly. Epidural web pad plica median dorsalis does not exist as shown by cryomicrotome sectioning. Hitherto what was believed to be epidural web is actually a homogenous semi fluid fat pad free of vessels or fibrous septation, attached by a pedicle to the epidural space. When air or contrast or Local Anaesthetics is injected, fat pad is compressed giving appearance as a connective tissue.

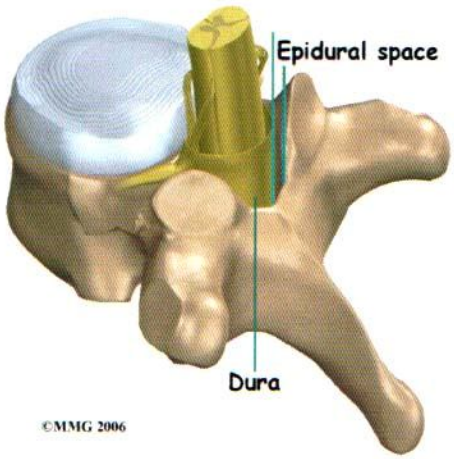
Anterior epidural space

Dura and posterior longitudinal ligament blend with annular ligament dividing it into vertical components at each vertebral level. It contains rich venous Plexus. Where the dura ends there is increasing amount of epidural fat especially from the lumbosacral region.

Cross Section of Vertebra



Lumbar Vertebra



Physiology of Local Anaesthetics in Epidural Space

Fate of Local Anaesthetics in the epidural space: Local Anaesthetics spreads longitudinally and horizontally.

The major roots of elimination of Local Anaesthetics from epidural space are

1. Uptake by blood vessels
2. Uptake in extra dural fat
3. Update in nervous tissue-spinal roots, spinal cord, spinal nerves
4. Leakage through intervertebral foramina.

Site of action of Local Anaesthetics

1. Spinal nerve roots with dural sleeves
2. Periphery of spinal cord
3. Mixed spinal nerve
4. Dorsal root ganglia

NEWER LOCAL ANAESTHETICS:

1) HCO3 addition: Increased speed of onset lmeq/l0ml
2) Carbonated Local anaesthetics
    - C02 diffuses into axons
    - increased ionized fraction inside cells
    - increased quality of block
    - increased speed of block.

Epidural Opioids

- Action on opioid receptors (μ) in substantia gelatinosa of spinal cord.
- Dose is 5 to 10 times greater than subarachnoid dose.
- No sympathetic blockade/motor blockade/loss of proprioception.
- Only analgesia which is dose related.
- Specific for visceral pain than somatic.

Epidural techniques

History:

First approach to epidural space was tried by Cathelin & Tuffier. It was refined by Fidel pages. Inl921, Dr.Jacques Forestier and Sicard identified the space by attaching a syringe of fluid to the needle advancing through the ligaments. Dogliotti in 1933 popularized the above test as "loss of resistance' test. Guieterrez and Soresi (1933) were the first to apply internal pressure differences to identify the space and they devised 'hanging drop' sign.

Identification of the epidural space:

(A) Hanging drop sign of Guiterrez :

The principle is based on hydrodynamic changes in epidural space.

Procedure to elicit hanging drop sign:-

- Ideal posture
- Good lighting
- Place a drop of fluid in needle hub on advancing the needle, with entry

into epidural space, one should watch for the in drawing of drop of fluid in hub.

- Positive sign is obtained properly, if puncture is made between C_7 and T_3 when patient is sitting with abdominal muscles relaxed.
- It is poorly appreciated in lower lumbar region when patient is sitting especially if they are crouched fully flexed.

Puncture Site	**Pressure in Epidural Space**	
	Sitting	**Lying**
1. Cervical	-3 to -9cmH_2O	-2 to -6 cm H_2O
2. Thoracic	-2 to-8 cmH_2O	-2 to -8 cm H_2O
3. Lumbar	+2 to -3 cm H2O	+2 to -6 cm H_2O

Epidural indicators for Negative pressure:-

1) U Tube Manometer
2) Aneroid manometer
3) Zorraquin's Bulb Indicator
4) Odom's indicator
5) Zelenka balloon indicator
6) Brook's indicator
7) Dawkin's gravity indicator
8) Auditory devices.

(B) Loss of resistance test of Forestier and Dogliotti :-

There is a sudden release of resistance to injection as advancing needle emerges from tough ligamenrum flavum into epidural space. This test needs a wide bore needle with large internal diameter ideally 16 Guage needle well suited, so that there is low internal resistances 5ml or 10ml syringes are preferable than 2ml syringe because with smaller syringes moderate pressure on plunger may discharge the contents before ligamentum flavum is reached making repeated refills necessary. Freely moving plunger is needed. Loss of Resistance can be done with fluid or air. Fluid is incompressible and the transition from complete resistance to loss of resistance is immediate. Air is compressible, so it is less ideal physical agent than fluid, but more reliable than fluid if glass syringes are used.

Approaches

Midline Approach - Hanging Drop Technique

Epidural needle with stylet is introducer in midline and in sagital plane to a depth of 2cm. Stylet is then withdrawn. A drop of analgesic solution is placed in hub of needle. Needle is now carefully advanced through the ligaments with hub and shaft held firmly by thumb and first three fingers of both hands, whiles the little fingers and hypothenar eminences and steadied against back. Since inspiratory movements transit a increment of negative pressure to epidural space, one should take advantage of this fact and advance the needle only during inspiratory phase of respiration.

Stop the advance of needle immediately as soon as these positive signs of epidural puncture manifest.

Paramedian Approach - Hanging Drop technique

Midline approach is technically difficult in mid thoracic region due to steep angulations and overlap of vertebral spines. In Paramedian approach, the needle is advanced 1.5 -2 cm lateral to the tip of vertebral spine at an angle of about 120° - 130° until gentle contact with lamina is made. Slide forward over the upper surface of lamina. A drop of Local Anaesthetic is placed in hub and needle gently walked along the bony surface of lamina until it is felt to glide over the cranial edge and through ligamentum flavum.

Midline Approach -Loss of Resistance Technique

It is easy in lumbar region L2-L3 interspinous spaces are sites of selection because the ligaments are broad and easily identified and they provide a solid sense of resistance to needle .After local infiltration , needle is introduced 2cm in midline. Stylet is removed.5ml or 10ml syringe with saline or air is firmly attached to the hub of needle. Constant pressure is exerted on the plunger of syringe. As the needle point emerges from ligamentum flavum into epidural space, resistance suddenly disappears.

Paramedian Approach -Loss of Resistance Technique;

Lumbar region relatively has an extra hazard of being easy to miss the deep bony landmarks of lamina and pass needle straight through interspinous space with consequent inadvertent dural tap; otherwise technique is similar to lateral approach for thoracic puncture as mentioned before.

COMPLICATIONS OF EPIDURAL ANALGESIA

Epidural analgesia is a technique that demands high level of precision and accurate clinical observation for routine success. The anesthesiologist should be familiar with complications associated with each phase of anesthetic and certain unrelated conditions and complications that may be erroneously attributed to epidural analgesia.

The complications can be studied under 3 heads;

TECHNICAL	Inadvertent dural puncture Massive subarachnoid injection Massive Subdural Injection Massive Epidural blockade Epidural intravenous injection Post dural puncture headache (PDPH) Backache Injection of wrong drug into epidural space

	Broken catheters
NEUROLOGICAL	Trauma to spinal cord or nerve roots Epidural hematoma Subdural hematoma Anterior Spinal Artery Syndrome Venous congestion causing spinal cord ischemia Bladder dysfunction
INFECTIVE	Epidural Abscess Subarachnoid infection Adhesive arachnoiditis of uncertain origin

Anticoagulants and Neuraxial Blocks

ASRA and Pain Medicine Consensus Conference Guidelines.

Thrombolytic drugs should be avoided for 10 days after puncture of non compressible vessels.

a) Patients receiving fibrinolytic and thrombolytic drug should be cautioned against receiving spinal or epidural blocks.
b) No definite recommendations for removal of neuraxial catheter in patients who unexpectedly receive thrombolytic therapy.

Patients on unfractionated Heparin

a) Subcutaneous mini-dose Heparin prophylaxis is not contraindicated for neuraxial blocks.
b) Combining neuraxial block with intraoperative Heparin injection in vascular surgery is acceptable with following cautions
    - To be avoided in patients with other coagulopathies.
    - Heparin can be given only one hour after needle placement.
    - Epidural catheters should be removed 2-4 hours after last heparin dose and restart after one hour.

Patients on Low Molecular Weight Heparin (LMWH)

The presence of blood during needle and catheter placement should delay initiation of LMWH therapy to 24 hours postoperatively. Preoperative LMWH.

- Epidural needle placement should atleast occur 10-12 hours after LMWH dose.
- Patients on higher doses (treatment) of LMWH will need atleast 24 hours before needle insertion.
    - Postoperative LMWH.
    - Twice daily LMWH.
- First dose of LMWH should be administered two hours after catheter removal.

Single daily dosing

- First postoperative LMWH dose is given 6-8 hours surgery.

- Indwelling catheters should be removed atleast 10-12 hours after the last dose of LMWH subsequent dosing should be given only 2 hours after catheter removal.

Patients on chronic anticoagulant therapy

- Stop anticoagulants atleast 4-5 days prior to planned procedure.
- PT/INR should be normalized prior to initiation of neuraxial block
- PT / INR should be measured if first dose was given more than 24 hours before or a second dose has been given.
- If thromboprophylaxis with warfarin is initiated neuraxial catheters should be removed when INR is < 1.5.

Patients on Antiplatelet Drugs

- NSAIDS-No added risk
- Thieonopyridine- Clopidogrel-discontinue atleast 7 days prior to procedure
- Ticlopidine -discontinue atleast 14 days prior to procedure.
- Group IIA /IIIB antagonist -contraindicated for 4 weeks after surgery.
- Patients on herbal drugs or newer anticoagulants- no definitive recommendation.

CONCEPT OF OPIATE SYSTEMS AND EPIDURAL OPIOIDS

Opioids injected into the epidural space spread into the surrounding tissues that include epidural fat and veins. Analgesia is produced through two mechanisms: spinal and supraspinal/systemic analgesia. Spinal mediated analgesia is produced as opioids diffuse into cerebrospinal fluid through the spinal meninges which depends through lipid solubility of the opioid. After entering CSF it interacts with spinal opioid receptors in the lamina II of dorsal horn of spinal cord and achieve antinociception via presynaptic reduction of afferent neurotransmitter release and post synaptic hyperpolarization of dorsal horn neurons. Supra spinal mediated analgesia is produced as opioids are absorbed into plasma and redistributed to the brainstem and blood stream.

CLASSIFICATION

Naturally occurring

- Morphine
- Codeine
- Papavarine
- Thebaine

Semisynthetic

- Heroin
- Dihydropmorphone
- Thebaine derivatives (eg. Etorphine, buprenorphine)

Synthetic

- Morphinan series (eg. Levorphanol, butorphanol)
- Diphenylpropylamine series (eg. Methadone)
- Benzomorphan series (eg. Pentazocine)
- Phenylpiperidine series (eg. Meperidine, fentanyl, sufentanil, alfentanil, remifentanil)
- Tramadol

Agonist-antagonist

- Pentazocine
- Butorphanol
- Nalbuphine
- Buprenorphine

Opioid receptors

Presence of opioid binding sites in nervous systems from radio ligand binding assay was described.

The μ receptors are located in both brain and spinal cord and thought to mediate variety of pharmacological effects of opioids.

Further μ receptors μ_1, μ_2 and μ_3 has been proposed.

Hydropathy analysis of primary structures of opioid receptors indicated opioid receptors possess seven transmembrane domains.

This is a characteristic structural feature of calcium protein coupled receptors.

Endogenous opioid peptide

Enkephalin, β endorphin and dynorphin were identified as endogenous agonist for δ, μ and K - opioid receptors respectively.

Pharmacologic actions of opioid and opioid receptors in animal models

	Actions of		
	Receptor	**Agonists**	**Antagonists**
Analgesia			
Supraspinal	δ, μ, κ	Analgesic	No Effect
Spinal	δ, μ, κ	Analgesic	No Effect
Respiratory function	μ	Decrease	No Effect
Gastrointestinal tract	μ, κ	Decrease transit	No Effect
Psychotomimesis	κ	Increase	No Effect
Feeding	δ, μ, κ	Increase Feeding	Decrease feeding
Sedation	μ, κ	Increase	No Effect
Diuresis	κ	Increase	
Hormone secretion			
Prolactin	μ	Increase release	Decrease release
Growth hormone	μ and /or δ	Increase release	Decrease release
Neurotransmitter release			
Acetylcholine	μ	Inhibit	
Dopamine	δ	Inhibit	

Mechanism of action

Analgesic effects of opioids arise from their ability to inhibit directly the ascending transmission of nociceptic information from spinal cord dorsal horn and to activate pain control circuits that descend from midbrain, via rostral ventromedial medulla (RVM) to spinal cord dorsal horn. Immuno histochemical studies and in situ hybridization analysis have demonstrated that opioid receptors are expressed in various areas in CNS.

These include the amygdala, the mesencephalic reticular formation, the periaqueductal gray matter (PAG) and rostral ventral medulla.

In spinal cord opioids act at synapses either presynaptically or post synaptically. Opioid receptors are abundantly expressed in substantia gelatinosa, where substance P release from primary sensory neuron is inhibited by opioids.

The decrease in neurotransmission occurs largely by presynaptic inhibition of neurotransmitter (acetylcholine, dopamine, nor -epinephrine, substance P) release although post synaptic inhibition of evoked activity may also occur.

The intracellular biochemical events initiated by occupation of opioid receptors with an opioid agonist are characterized by increased potassium conductance (leading to hyper polarization), calcium channel activation or both which produce immediate decrease neurotransmitter release.

Opioid receptors exist on peripheral ends of primary afferent neurons and their actuation may either directly decrease neurotransmission or inhibit release of excitatory neurotransmitters such as substance P. Depression of cholinergic

transmission in CNS as a result of opioid induced inhibition of acetylcholine release from nerve endings may play a prominent role in analgesic and other side effects of opioid agonists.

Opioid effects are mediated by opioid receptors which are macromolecules composed of 2 parts-

i) A binding site, which interacts with opioid molecules, and
ii) Triggering molecule mechanism, which activates a number of sequential biochemical reactions that lead to final neuronal effect.

Mechanism of spinal opioid action

1. At first order neuron level (presynaptically) it blocks release of neurotransmitter substance P thereby acting as a neuromodulator by changes in calcium channel.
2. At second order neuron level (post synaptically) it
    a. Hyperpolarizes neuronal membrane by alterations in potassium channel and increases the excitatory threshold.
    b. Blocks summation of excitatory post synaptic potentials.
    c. Prevents expansion of receptive fields
    d. Prevents neuronal gene expressions

Side effects of opioids

1. Respiratory depression

This is biphasic phenomenon with an initial respiratory depression due to

systemic absorption from epidural depot of narcotics often occurring within first hour of injection and much delayed (6-8 hours) depression due to rostral spread of drug.

The incidence of ventilatory depression requiring intervention after conventional doses of neuraxial opioids is about 1% which is the same as that after conventional doses of IV or IM opioids.

Factors increasing the magnitude of opioid induced respiratory depression

- High dose
- Sleep
- Old Age
- CNS depressant
    - Inhaled anesthetics, alcohol, barbiturates, benzodiazepines
- Renal insufficiency
- Hyperventilation, hypocapnia
- Respiratory acidosis
- Decreased clearance
    - Reduction of hepatic blood flow
- Secondary peaks in plasma opioid levels
- Reuptake of opioids from muscle, lung, fat and intestine
- Pain

Bailey PL [2] (1985) stressed that older patients are more sensitive to anesthetic and respiratory effects of opioids. They have —more frequent apnea, periodic breathing and upper airway obstruction after Morphine than young adults.

Older patients experience higher plasma concentrations of opioids administered on weight basis.

Bailey PL (1990) also stressed that respiratory depressant effects of opioids are increased when administered with CNS depressants, including potent inhaled anesthetic, alcohol, barbiturates, benzodiazepines and intravenous sedatives and hypnotics.

According to Pelligrino DA (1989) more potent respiratory depressant properties of Morphine metabolite, morphine 6 glucoronide becomes evident as it is accumulated.

Hypocapnic hyperventilation has been shown to enhance and prolong post operative respiratory depression after Fentanyl because of increased unionized Fentanyl and decreased cerebral blood flow with hypocarbia.

Koehntop DE [15] (1986) noted the occurrence of significant secondary peaks and fluctuations in plasma opioid level during elimination phase.

In contrast to risk of respiratory depression when these drugs are administered in post operative period, the administration of these drugs for chronic pain control in patients with terminal malignancy has been remarkably free of respiratory depression.

2. Urinary Retention

Like respiratory depression urinary retention seems to be more frequent when epidural opioids are administered in post operative period with incidence of 22%. On the contrary this problem is not seen in cancer patients.

Rawal et al [24] suggested that urinary retention was likely due to interaction of opioid with opioid receptors located in sacral spinal cord. This promotes inhibition of sacral parasympathetic nervous system outlflow, which causes detrusor muscle relaxation and increase in maximum bladder capacity leading to urinary retention.

Rawal et al [24] also suggested that Morphine causes marked detrusor muscle relaxation within 15 minutes of injection that persists for upto 16 hours it is readily reversed with naloxone.

3. Nausea and vomiting

Incidence is approximately 30%. Opioids decrease gastro intestinal motility and after lower esophageal sphincter activity, resulting in sphincter relaxation. Gastric emptying is delayed by opioids via supraspinal and spinal as well as peripheral mechanism.

Opioid stimulate chemoreceptor trigger zone in area postrema of medulla possibly though delta receptors leading to nausea and vomiting. These are frequent side effects associated with use of epidural Morphine.

Booker (1980), Magora (1980) suggested that nausea and vomiting were seen particularly in obstetric patients after single dose of epidural opioids.

Welchem [33] observed that nausea and vomiting were associated with Fentanyl infusion though incident was lower with epidural Fentanyl than epidural morphine.

Gedney JA [8], White MJ (1992), Ozalp G(1998) suggested that "the use of Fentanyl or in combination with a local anesthetic in an epidural infusion is associated with lower incidence of nausea and limiting compared with infusions using Morphine.

4. Pruritis

Incidence 15 to 18%. Chaney MA [6] suggested that pruritis is related to central activation of "itch center" in medulla or opioid receptors in trigeminal nucleus or nerve roots with cephalad migration of opioid.

Gedney JA[8], Ozalp g (1998) and Bucklin BA (2002) suggested that epidural infusion of Fentanyl above or as part of local anesthetic opioid combination appear to be generally associated with lower incidence of pruritis compared with Morphine.

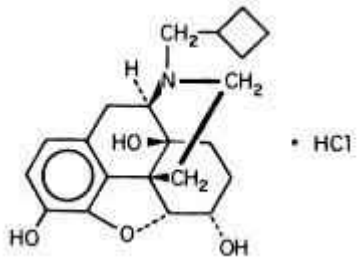
Pruritis is more likely to be localized to face, neck or upper thorax. It is more likely to occur in obstetric patients due to interaction of estrogen with opioid receptors. It may or may not be dose dependent.

Naloxone is effective in relieving opioid induced pruritis.

PHARMACOLOGY OF NALBUPHINE

Nalbuphine is classified as a synthetic opiod agonist-antagonist which is chemically related to the opiod antagonist, naloxone and potent opiod agonist oxymorphone.

It is soluble in water and ethanol. It acts as a potent antagonist at mu receptors.10mg of nalbuphine is equianalgesic to 10mg morphine with less respiratory depression due to its ceiling effects at incremental doses.



PHARMACODYNAMICS:

CARDIOVASCULAR SYSTEM

1) No effect on cardiac contractability.
2) Not much effect on systemic blood pressure, pulmonary arterial pressure.
3) Decreases cardiac workload.
4) Not much change in heart rate.

RESPIRATORY SYSTEM

1) Respiratory depression exhibits ceiling effect with incremental doses.
2) antagonizes respiratory depression caused by morphine due to mu antagonist action.

CENTRAL NERVOUS SYSTEM

1) Dizziness
2) Headache
3) At higher doses causes sedation and dysphoria.

GASTROINTESTINAL SYSTEM

1) Nausea
2) Vomiting
3) Dyspepsia

ENDOCRINE

Attenuation of stress response

PHARMACOKINETICS

Pka	-	7.45
Plasma $t_{1/2}$	-	5 hours
Elimination $t_{1/2}$	-	2.4 hours
Duration of action	-	3 to 6 hours

It is metabolized by liver and eliminated by kidney.

ADVANTAGES OF EPIDURAL NALBUPHINE

1) Minimal CSF spread
2) Rapid onset
3) Rapid analgesia
4) Decreased side effects
5) Ideal for post operative and chronic pain management
6) Decrease incidence of pruritis if used along with morphine

DISADVANTAGES

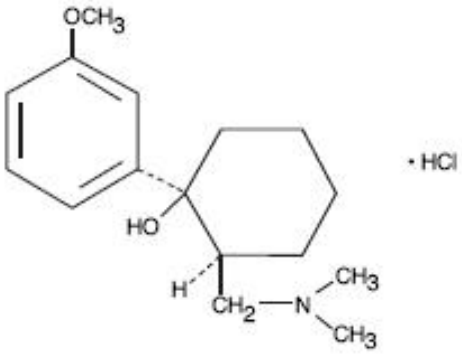
1) Sedation may occur at high doses
2) Brief single dose analgesia

Factors associated with respiratory depression:

Elderly, poor general condition, concomitant use of other drugs, use of hydrophilic opiods

PHARMACOLOGY OF TRAMADOL

It is a centrally acting opiod which has moderate affinity for mu receptors and weak affinity for kappa and delta receptors. It also inhibits neuronal uptake of norepinephrine and serotonin. Tramadol is available as a racemic mixture of two enantiomers. o-desmethyltramadol is a metabolite of tramadol as it is metabolized by hepatic p 450 enzyme.



PHARMACOKINETICS:

- Elimination $t_{1/2}$-6 hours.
- Metabolite of tramadol has elimination $t_{1/2}$-7.5 hours
- Duration of analgesia-6hours.

SIDE EFFECTS:

Nausea, vomiting, dizziness, dry mouth and sedation.

Respiratory depression is comparatively less compared to morphine.

DISADVANTAGES:

Interacts with coumarin anti coagulants.

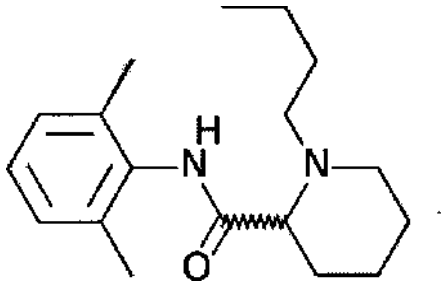
PHARMACOLOGY OF BUPIVACAINE

HISTORY

It is a amide linked Local Anesthetic synthesized in 1957 by B.A.F.Ekenstam and introduced in to clinical practice by Talivero in 1963.

STRUCTURE

An amide linked Local Anaesthetic having aromatic moiety (benzene ring) which offers lipophilicity at one end of molecule. It is linked by an amide to a tertiary amine which is hydrophilic on the other end of the molecule.



Bupivacaine

It displays stereo-isomerism marketed as a racemic mixture containing optically active enantiomers; R+S. S enantiomer has been noted to have a slightly longer duration of action yet lower systemic, toxicity when compared to R form.

Mechanism of Action

The base form is in equilibrium with cationic form outside the axoplasmic membrane. Base form diffuses inside the cell and equilibrates with cationic form. It then reaches the Local Anesthetic tor in Na channel by reversing channel

pore while it is in the open lite. It prevents sodium channels moving intracellularly.

In addition to the simple sodium channel blockade it also affects second messenger system such as adenylate cyclase and guanylate cyclase and also inhibits synaptic transmission by modification of postsynaptic receptor or pre-synaptic Calcium channel blockade in epidural or Subarachnoid block.

PHYSIO-CHEMICAL PROPERTIES

Molecular weight	-	288
Potency ratio	-	15
Toxicity ratio	-	10
pka	-	8.16
Protein binding (%)		
Maternal	-	95
Fetal	-	66
% of non ionized at		
pH 7.4	-	17
pH 7.2	-	11
Partition co-efficient		
(25 degree celsius, pH 7.4)	-	346
Anesthetic index	-	3 - 4.0

PHARMACOKINETICS OF EPIDURAL BUPIVACAINE

The uptake of Local Anesthetic into blood vessel in the area where it has been deposited and its subsequent transfer into systemic circulation is referred to as systemic absorption.

A biphasic absorption phase has been found for this epidural bupivacaine. The rapid initial absorption following epidural Bupivacaine is most likely related to high concentration gradient between the drugs in solution and in the blood. In addition, profound increase in epidural flood flow observed during epidural administration of Bupivacaine may contribute to its fast initial absorption rate.

Later on, after Local Anesthetic has been taken up into local tissues such as epidural fat, absorption will become dependent on tissue blood partitioning resulted in marked slowing of absorption. Estimated total fraction of dose ultimately absorbed into general circulation is 0.94. with mean absorption time of 8hrs.

Absorption of Local Anesthetic is discretely related to amount of drug injected, vascularity, site injected and tissue binding of local anaesthetic at injection site. Bupivacaine will produce low Cmax than less potent and less soluble agents.

DISTRIBUTION

It refers to delivery of absorbed drugs to various parts of body. Distribution of Local Anesthetic has special emphasis in pregnant patients because the feto placental unit also is exposed to it.

Elimination half life	-	162mins
Volume of distribution	-	73L
Clearance	-	0.61/min
Hepatic extraction	-	0.4

BIO DEGRADATION AND ELIMINATION

Bupivacaine is metabolized in liver. Two major factors controlling clearance of amide-linked Local Anesthetic are hepatic blood flow and hepatic function and principal pathways being N-de-alkylation, aromatic hydroxylation and amide hydrolysis.

ADVERSE EFFECTS

1. Central Nervous Toxicity

Potentially toxic blood level can occur when a drug is injected intravenously, intra arterially or a large dose of drug is injected into highly vascular area. Risk of Central Nervous toxicity is more because Bupivacaine is a highly protein bound drug. Pregnancy is associated with 30% reduction in protein binding. This allows for higher brain level of Bupivacaine for a given dose of drug.

Signs:

Slurring of speech, jerky movements, tremors, hallucinations, seizures.

Cardiovascular toxicity:

Bupivacaine being four times more potent than lignocaine shows dose dependent depression of myodcardial contractility.It also shows dose dependent depression of conduction and velocity of all conducting tissues leading to progressive prolongation of ventricular conduction.Pre disposition to reentry phenomenon may be followed by sudden onset of VF.These effects is due to its high affinity for cardiolipin.Toxic plasma concentration for cardiotoxicity is 4 to 5 micro g/ml.

REVIEW OF LITERATURE

The introduction of epidural catheters has been used to provide long lasting pain relief, which led to formation of acute pain services. The special advantages of epidural opioids was the synergistic effect they exhibited with local anesthetics allowing a marked decrease in dose of both drugs to achieve same level of analgesia.

1. Veena Chatrath et al. Comparative evaluation of bupivacaine hydrochloride with nalbuphine versus bupivacaine with tramadol for postoperative analgesia in lower limb orthopedic surgeries under CSE anesthesia to know the quality of analgesia, incidence of side effects, surgical outcome and level of patient satisfaction. A prospective, randomized and double-blind study was conducted involving 80 patients of American Society of Anesthesiologists physical status I and II coming for elective lower limb orthopedic surgeries carried under spinal anesthesia. Anesthesia was given with 0.5% of 2.5 ml bupivacaine intrathecally in both the groups. Epidurally 0.25% bupivacaine along with 10 mg nalbuphine (group A) or tramadol 100 mg (group B) diluted to 2 ml to make a total volume of 10 ml was administered at sensory regression to T10.

Hemodynamic parameters such as pulse rate, BP, SpO_2, respiratory rate were recorded and monitoring was done every 5 min for first 30 min and then every 15 min till the end of the surgery in both the groups. Patients were assessed using VAS score every half hourly for the first 2 h then 4, 8, 12, 16 and 24 h after giving top up dose of the test drug for intensity of pain, HR, BP, respiratory rate

and sedation score. The patient's characteristics were analyzed using the Chi-square test applied to nonparametric data while the intergroup comparison of the parameter data was done using the unpaired *t*-test. The demographic characteristics of patients were comparable between the two groups regarding mean age, weight ASA grading, diagnosis and duration of surgery. There was no significant difference in HR , systolic BP, diastolic BP and SpO_2 during intraoperative period among the two groups. They concluded that both nalbuphine and tramadol were effective for postoperative analgesia when used epidurally in patients undergoing lower limb orthopedic surgery. However, nalbuphine group was better in terms of better quality of surgical analgesia, lesser incidence of side-effects and complications e.g. nausea, vomiting and sedation and better patient satisfaction score as compared to tramadol group.

2.B Jyothi et al, A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. The effects of intrathecal 0.5% hyperbaric bupivacaine with nalbuphine hydrochloride at three different doses (0.8, 1.6, and 2.4 mg) were studied and compared with 0.5% hyperbaric bupivacaine alone in 100 patients belonging to ASA grade I and II who underwent lower limb orthopedic and lower abdominal procedures including general surgeries and gynecological surgeries. The four groups of patients A, B, C, and D included in the study did not differ significantly with respect to age, sex, body weight, height, type, and duration of surgery. The mean time of onset of sensory blockade between the groups is comparable with the *P* value >0.05

which is statistically not significant. Two segment regression of sensory blockade is significantly prolonged by addition of intrathecal nalbuphine as seen with Groups B, C, and D when compared with group A with bupivacaine alone. The duration of analgesia was significantly prolonged with the addition of nalbuphine as compared with bupivacaine alone.The mean VAS score in group A is higher 4.08 ± 0.5 when compared with the VAS score in groups B, C, and D 3.4 ± 0.4, 3.5 ± 0.5, and 3.5 ± 0.5, respectively. Statistical analysis shows that there is significant difference between Groups B, C, and D when compared with Group A. The quality of analgesia is good with nalbuphine groups compared with bupivacaine alone.

3. Schnabel A et al, has done a study on tramadol for postoperative pain relief in children for different surgeries. Because of a relatively wide therapeutic window and a ceiling effect with a lower risk for severe adverse events (for example respiratory depression) tramadol is a widely used opioid in children. To assess the effectiveness and side effect profile of tramadol for postoperative pain relief in children and adolescents undergoing different surgical procedures. In this study tramadol was compared with placebo and the need for rescue analgesia was reduced in tramadol group monitored in pacu. (RR 0.40; 95% CI 0.20 to 0.78; low quality evidence). They demonstrated that tramadol administration might provide appropriate analgesia when compared to placebo; this is based on results showing reduced rescue analgesia in children treated with tramadol compared to placebo.

4. Tarkkila p et al, compared the respiratory effects of tramadol and pethidine. The respiratory effects of intravenous (i.v.) pethidine (0.6 mg kg-1) and tramadol (0.6 mg kg-1) were compared in 36 ASA Grade I-II patients in a placebo-controlled double-blind study. After induction of anaesthesia with propofol followed by suxamethonium-facilitated endotracheal intubation, the patients spontaneously breathed halothane in 70% nitrous oxide and oxygen via a non-rebreathing valve. Inspiratory and expiratory oxygen, and end-tidal carbon dioxide concentrations , tidal volume , minute volume of ventilation and respiratory rate were monitored by a side-stream spirometry at an end-tidal halothane of 0.3%. The recordings were collected before surgery. Pethidine caused significant respiratory depression seen as an increase in fractional inspiratory-expiratory oxygen difference and ETCO2 and as a decrease in minute volume and respiratory rate. However, the effects of tramadol were similar to those of a placebo. Tidal volume was not affected by any study drug. In conclusion, tramadol 0.6 mg kg-1 was shown not to be associated with respiratory depression, unlike equipotent dose of pethidine .

5. Mukherjee A et al, has studied the use of nalbuphine as an adjuvant for sub arachanoid block. The purpose of his study was to establish the effectiveness of intrathecal nalbuphine as an adjuvant, comparing three different doses and to determine the optimum dose with prolonged analgesic effect and minimal side-effects. In this prospective, randomized, double-blinded, controlled study, 100 ASA I and II patients undergoing lower limb orthopedic surgery under subarachnoid block (SAB), were randomly allocated to four

groups: A, B, C and D, to receive 0.5 ml normal saline (NS) or 0.2, 0.4 and 0.8 mg nalbuphine made up to 0.5 ml with NS added to 0.5% hyperbaric bupivacaine 12.5 mg (total volume 3 ml), respectively. The onset of sensory and motor blockade, two-segment regression time of sensory blockade, duration of motor blockade and analgesia, visual analogue scale (VAS) pain score and side-effects were compared between the groups.

Two-segment regression time of sensory blockade and duration of effective analgesia was prolonged in groups C (0.4 mg nalbuphine) and D (0.8 mg nalbuphine) ($P<0.05$), and the incidence of side-effects was significantly higher in group D ($P<0.05$) compared with the other groups.

Nalbuphine used intrathecally is a useful adjuvant in SAB and, in a dose of 0.4 mg, prolongs postoperative analgesia without increased side-effects.

6. Roussel A et al, has studied the effects of intrathecal fentanyl on duration of bupivacaine spinal blockade for outpatient knee arthroscopy. The purpose of this study was to determine if intrathecal fentanyl speeds the onset and prolongs the duration of sensory and motor block, prolongs the duration of postoperative analgesia, or increases the incidence of adverse effects in patients undergoing spinal anesthesia for outpatient knee arthroscopy. Fifty patients were randomized to receive 12 mg of hyperbaric bupivacaine 0.75% with 25 micrograms (0.5 mL) of fentanyl (group 1) or 12 mg of hyperbaric bupivacaine 0.75% with 0.5 mL of preservative-free normal saline (group 2). One-tailed t tests were used to determine differences in onset and duration of sensorimotor block and postoperative analgesia. No differences were found in onset and

duration of sensory or motor block. Group 1 experienced significantly better postoperative analgesia lasting more than 3 hours longer than analgesia for group 2. Group 1 demonstrated significantly more pruritus, but there were otherwise no differences.Their study concluded that fentanyl does not enhance the onset and duration of sensory or motor block produced by 12 mg of intrathecal bupivacaine. Fentanyl, however, prolongs postoperative analgesia and increases the risk of pruritus.

7. J.A.Alhashemi et al, has studied the effect of intrathecal tramadol administration on postoperative pain after transurethral resection of prostate. In this double-blind, placebo-controlled study, the effect of intrathecal tramadol administration on pain control after transurethral resection of the prostate (TURP) was studied.Sixty-four patients undergoing TURP were randomized to receive bupivacaine 0.5% 3 ml intrathecally premixed with either tramadol 25 mg or saline 0.5 ml. After operation, morphine 5 mg i.m. every 3 h was administered as needed for analgesia. Postoperative morphine requirements, visual analogue scale for pain at rest (VAS) and sedation scores, times to first analgesic and hospital lengths of stay were recorded by a blinded observer. There were no differences between the groups with regard to postoperative morphine requirements (mean (SD): 10.6 (7.9) *vs* 9.1 (5.5) mg, *P*=0.38), VAS (1.6 (1.2) *vs* 1.2 (0.8), *P*=0.18) and sedation scores (1.2 (0.3) *vs* 1.2 (0.2), *P*=0.89). Times to first analgesic (6.3 (6.3) *vs* 7.6 (6.2) h,*P*=0.42) and length of hospital stay (4.7 (2.8) *vs* 4.4 (2.2) days, *P*=0.66) were similar in the two groups. Intrathecal tramadol was not different from saline in its effect on

postoperative morphine requirements after TURP.

8.) Anil P singh et al, studied the postoperative efficacy of epidural tramadol as adjuvant to ropivacaine in adult upper abdominal surgeries. Ninety patients planned for upper abdominal surgery under general anesthesia were randomized into three equal groups to receive epidural drug via epidural catheter at start of incisional wound closure: Group R received ropivacaine (0.2%); Group RT1 received tramadol 1 mg/kg with ropivacaine (0.2%); and RT2 received tramadol 2 mg/kg with ropivacaine (0.2%). Duration and quality of analgesia (visual analog scale [VAS] score), hemodynamic parameters, and adverse event were recorded and statistically analyzed.

Mean duration of analgesia after epidural bolus drug was significantly higher in Group RT2 (584 ± 58 min) when compared,they concluded that tramadol 2 mg/kg with ropivacaine (0.2%) provides more effective and longer-duration analgesia than tramadol 1 mg/kg with ropivacaine (0.2%).ith RT1 (394 ± 46 min) or R Group (283 ± 35 min). VAS score was always lower in RT2 Group in comparison to other group during the study. Hemodynamic parameter remained stable in all three groups. The incidence of nausea and vomiting was observed in 3% patients in Group R, 10% patients in Group RT1, and 16% in Group RT.

9. Gurkan Y et al [9], (2005) compared the analgesic efficacy and side effects of Bupivacaine - Fentanyl and Bupivacaine - Morphine combinations for Patient Controlled Epidural Analgesia. Post operative analgesia was provided in both groups. The incidence of pruritis and respiratory depression was higher in

Bupivacaine-Morphine group, who responded to IV Naloxone.

10. Dhalae[6], Shelgoankar, Akulwar (2000) compared epidural Bupivacaine with Fentanyl of three different doses 25, 50 and 75ug respectively and epidural 0.5% Bupivacaine for postoperative of analgesia in elective lower limb orthopedic procedures and lower abdominal surgeries. They found that 50ug Fentanyl with 0.5% Bupivacaine was a better choice for post operative analgesia with acceptable side effects.

11. Sinatra [5] R.S Swamidas et al (1998) showed that Fentanyl lacks rostral spread. This is due to rapid incorporation into epidural fat and vascular clearance from epidural and intrathecal sites of deposition. Dermatomal spread of lipophilic opioids appear to be directly related to dural surface area in contact with drug and may be increased following administration of larger volumes of solutions. The duration of action is dose dependant with lipid soluble agents such as Fentanyl and Meperidine, having shorter time course than more polar agent such as Morphine.

12.Tsui SL et al (1997) concluded that epidural infusion of Bupivacaine 0.0625% and Fentanyl 3.3 ug/ml provided better analgesia , no hypotension and no respiratory depression when compared with Patient Controlled Intravenous Morphine after gynecological laparotomy.

13.Sakaguchi H et al [10], (1995) suggested that Bupivacaine-Fentanyl continuous infusion is superior to Morphine bolus in post operative epidural analgesia.

14. Nakamura T et al [8] (1994) suggested that post operative

continuous epidural analgesia is more effective if entrance of noxious stimuli into central neural system in prevented by pre incisional epidural block. He studied the effect of epidural analgesia administered before or during surgery on post operative pain relief using continuous epidural infusion of mixture of local anesthetics and narcotics.

15.Badner NH [13], Bandari R, Komar WE (1994) suggested that 0.125% Bupivacaine improves the analgesia of epidural infusion of Fentanyl when used following abdominal or thoracic surgery and resulted in minimal sensory-motor disturbance.

16. Belzaena S .D (1992) observed clinical effects of intrathecal / epidural opioids in patients undergoing cesarean section. In their study, Morphine a lipopholic opioid agonist when administered via spinal / epidural route provides longer lasting analgesia than lipophilic opioid like Fentanyl. Fentanyl alone or when administered together with local anesthetic has faster onset compared with Morphine. In further study he concluded that combination of Bupivacame and low dose (0.25ug/kg) of intrathecal Fentanyl provided excellent surgical anesthesia and very few undesirable side effects for women undergoing cesarean section.

17. Berti M et al [12] (1988) compared epidural infusions of Bupivacaine-Fentanyl and Bupivacaine-Morphine mixtures for post operative pain relief after total hip replacement and concluded that Bupivacaine-Morphine or Bupivacaine-Fentanyl mixtures provided similar pain relief. Patients receiving Morphine should marked decrease in SpO2 than Fentanyl group.

MATERIALS AND METHODS

Sixty patients with femoropopliteal occlusion admitted in the Department of Vascular surgery, Government General Hospital, Madras Medical College, have been taken up for study. A randomized prospective clinical trial has been conducted after obtaining the informed consent.

Grouping

Patients with rest pain were grouped into A and B.

- Group A- patients received 2.5ml of 0.5% hyperbaric bupivacaine intrathecally followed by intermittent bolus doses of 0.25% Bupivacaine with 10mg nalbuphine through epidural catheter.
- Group B- patients received 2.5ml of 0.5% hyperbaric bupivacaine intrathecally followed by intermittent bolus doses of 0.25% Bupivacaine with 50mg tramadol through epidural catheter .

  Pain scores using Visual Analogue Scale and vitals in both the groups were noted.

Type of study -Randomized clinical trial

Inclusion criteria

- Age : 18 years and above
- Weight : BMI < 30 Kg/m2
- ASA : I , II, III
- Surgery : Elective
- Mallampati scores : I & II
- Who have given valid informed consent.

EXCLUSION CRITERIA:

- Patient's refusal.
- Allergy to local anaesthetics
- Coagulopathy
- Systemic or local sepsis
- H/O seizures and any neurological deficit
- Psychiatric diseases
- Not satisfying inclusion criteria
- Vertebral abnormalities
- Emergency procedures

Methods

Patients with rest pain were assessed by taking good history, physical examination and investigations pre procedure.

Cardiovascular System

Degree of Coronary Artery Disease,presence of valvular disease and ventricular function is assessed by ECG and ECHO.

Respiratory System

History of smoking habits is elicited. Breath holding time, Chest x ray PA view, Pulmonary Function Test were done.

Central Nervous System

History of Transient Ischemic Attacks, declining mental function, and tested for cognitive function .Spine and motor power of lower limbs were documented.

Renal system – evaluated to rule out renal failure and renal artery stenosis.

Hematological System-Hemoglobin, cell counts , platelet count, Bleeding Time, Clotting Time.

General examination included general condition, blood pressure measurement, pulse rate respiratory rate, SPO2, Visual Analogue Scale using a 10 cm scale marked one to ten with 'no pain' at the zero end and maximum pain at other end.

Medications- T.Aspirin, T.Clopilet, Injection Heparin. T.Clopilet was stopped 7 days before. UFH stopped 6 hours before the procedure.

- Investigations included
    - Hemoglobin/packed cell volume
    - Platelet count
    - Bleeding time and Clotting time.
    - Total count, differential count, ESR
    - Random Blood Sugar
    - Renal function test
    - Serum electrolytes
    - Electrocardiogram
    - Echocardiogram.
    - Chest X ray Postero Anterior view.
    - Urine for Albumin and sugar

- Pre-procedure visit
    - To get rapport with patients and reassurance. To make sure the patient has been completely evaluated and medications like heparin and clopilet have been stopped.
- Assessment of airway, neck movements

Procedure

- Patient shifted to operation theater
- Monitors were connected – Non Invasive Blood Pressure, SP02, ECG
- Pre-procedure Heart Rate, Blood Pressure, Respiratory Rate, SP02, Visual Analogue Scale, Motor Power of Lower Limbs assessed.
- All emergency resuscitative drugs including injection Naloxone were kept ready.
- Resuscitative equipments like intubating laryngoscope with suitable blades, appropriate size endotracheal tubes, laryngeal Mask Airways were kept ready.
- Boyles machine was checked for proper functioning
- Epidural set consisting of sterile tray, sterile gauze and towel, glass syringe 2ml, 5ml, 10ml with hypodermic needles 22/23/24G, sponge holding forceps, Qunicke Babcock needle(25G), epidural Tuohy needle 16G with catheter 90cm (18G) were made available.
- Patients cannulated with 18G cannula and preloaded with 15-20ml/kg of crystalloid solution prior to block.
- Aseptic precautions were followed throughout the procedure.

Technique

- After re- explaining to the patient, patient positioned
- Patient skin over back was cleansed with betadine and draped.
- Intervertebral space using highest point of iliac crest was identified.
- Skin and subcutaneous tissue overlying the midline of space was infiltrated with 2ml if 2% lignocaine using 22G hypodermic needle.
- 16G Tuohy needle was introduced till the interspinous ligament and stylet was removed.
- A 5ml glass syringe with air filled upto 2ml was attached to hub of needle and advanced cautiously to identify the epidural space using LOR technique.
- After the epidural space was identified, catheter was inserted with the tip at L_3, L_4 and fixed in position.
- Following skin infiltration with local anaesthetic,2.5ml of 0.5% bupivacaine given intratheally.
- Randomly patients were given intermittent boluses epidurally when sensory regression of T_{10} was reached.

Thirty patients were given 8ml of 0.25% Bupivacaine with 10mg nalbuphine. Vitals monitored to check for signs of complication. The subsequent bolus doses were repeated when visual analogue scale scores showed 4.

Thirty patients were given 8ml of 0.25% bupivacaine with 50mg tramadol. Vitals monitored to check for signs of complication. The subsequent bolus doses were repeated when visual analogue scale score was 4.

Monitoring

Heart rate, Blood Pressure (systolic and diastolic), respiratory rate, Sp02 were initially recorded every minute for 10 minutes, every 5 minutes for next 30 minutes , every 30 minutes for next 1 hour, hourly for 12 hours, 6th hourly for 72 hours. VAS scores were recorded 2 hourly.

Sensory blockade

Onset of analgesia - Time taken from injection of local anesthetic with opioid to start of loss of sensation to pin prick was noted in the both groups.

Motor blockade – assessed with Bromage Scale

0 - No paralysis

1 - inability to raise extended leg

2 - inability to flex knee

3 - inability to flex ankle and big toe

Complications

Patients were monitored for hypotension, bradycardia, urinary retention, respiratory depression, pruritis and nausea, vomiting.

OBSERVATION

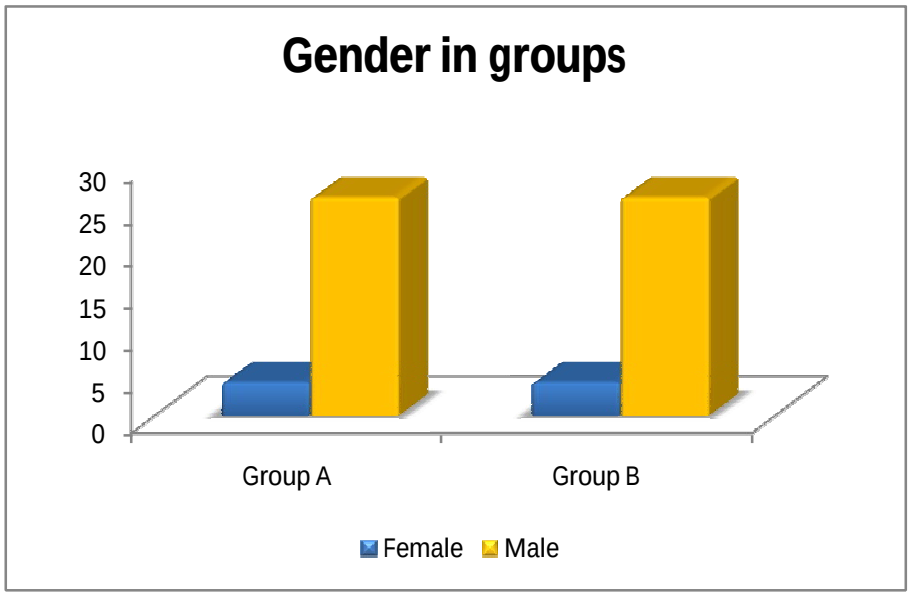
This study was conducted at madras medical college, on patients with femoropopliteal disease admitted in department of vascular surgery MMC,Chennai.The comparison of analgesic efficacy of 0.25% Bupivacaine with 10mg nalbuphine with 0.25% Bupivacaine with 50mg tramadol administered epidurally was done.

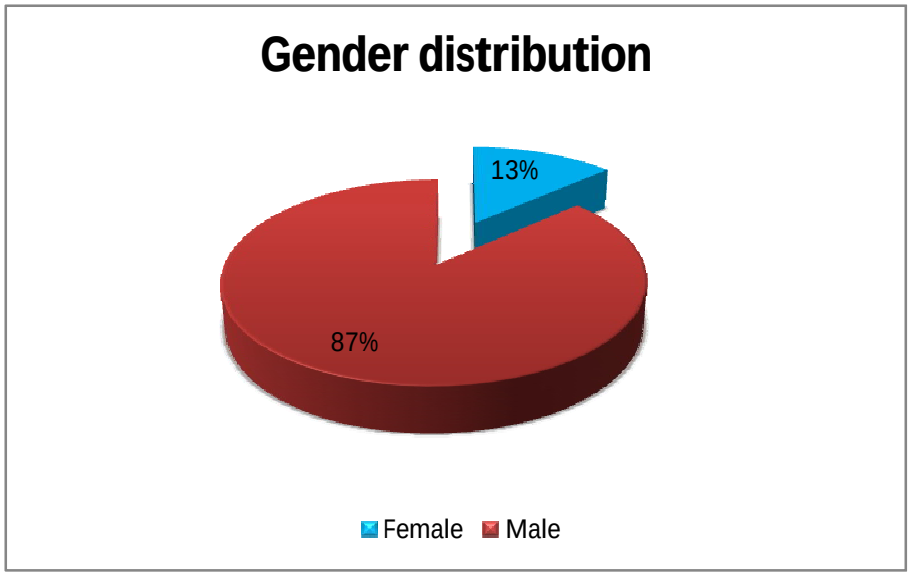
STATISTICAL ANALYSIS

The parameters systolic blood pressure (SBP), diastolic blood pressure (DBP), Pulse Rate (PR), Visual Analogue Scale (VAS) have been evaluated on 30 patients each admitted to the two groups. The parameters are compared at different time points within the same treatment group and between the treatment groups. giving due considerations to the two treatment groups and setting up a null hypothesis that both groups offer the same benefit, the parameters are tested for statistical significance. The paired t-test statistics was used.

The parameters heart rate, systolic blood pressure, diastolic pressure, mean arterial pressure were recorded every 5min for 1 hour, every hour for 6 hours and 4^{th} hourly thereafter. For statistical calculations the observations same time points have been considered.

GENDER PREDILECTION





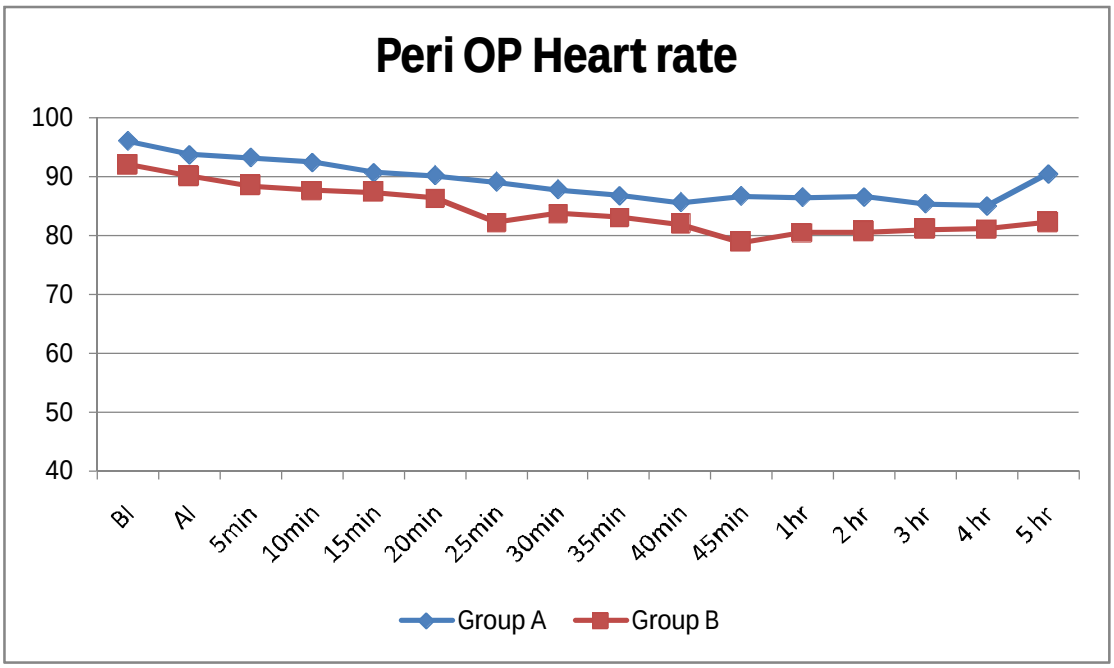
	Group A	Group B
Female	4	4
Male	26	26

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
PERIOP HEART RATE-BI	GROUP A	30	96.07	5.433	.992
	GROUP B	30	92.00	7.400	1.351
PERIOP HEART RATE-AI	GROUP A	30	93.77	5.283	.965
	GROUP B	30	90.03	6.734	1.229
PERIOP HEART RATE-5	GROUP A	30	93.23	5.923	1.081
	GROUP B	30	88.40	6.836	1.248
PERIOP HEART RATE-10	GROUP A	30	92.47	6.263	1.143
	GROUP B	30	87.70	7.183	1.311
PERIOP HEART RATE-15	GROUP A	30	90.70	6.086	1.111
	GROUP B	30	87.37	6.631	1.211
PERIOP HEART RATE-20	GROUP A	30	90.20	5.647	1.031
	GROUP B	30	86.43	6.892	1.258
PERIOP HEART RATE-25	GROUP A	30	89.07	5.452	.995
	GROUP B	30	82.30	16.263	2.969
PERIOP HEART RATE-30	GROUP A	30	87.80	5.517	1.007
	GROUP B	30	83.80	6.754	1.233
PERIOP HEART RATE-35	GROUP A	30	86.87	5.507	1.005
	GROUP B	30	83.10	7.136	1.303
PERIOP HEART RATE-40	GROUP A	30	85.60	5.654	1.032
	GROUP B	30	81.90	6.172	1.127
PERIOP HEART RATE-45	GROUP A	30	86.70	5.559	1.015
	GROUP B	30	78.90	15.562	2.841
PERIOP HEART RATE-1 hr	GROUP A	30	86.53	5.393	.985
	GROUP B	30	80.50	6.756	1.233
PERIOP HEART RATE-2 hr	GROUP A	30	86.63	5.048	.922
	GROUP B	30	80.67	6.635	1.211
PERIOP HEART RATE-3 hr	GROUP A	30	85.40	5.593	1.021
	GROUP B	30	81.07	6.893	1.258
PERIOP HEART RATE-4 hr	GROUP A	30	85.07	6.034	1.102
	GROUP B	30	81.20	6.677	1.219
PERIOP HEART RATE-5 hr	GROUP A	15	90.53	7.090	1.831
	GROUP B	25	82.20	7.382	1.476

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
PERIOP HEART RATE-BI	Equal variances assumed	4.584	.036	2.426	58	.018	4.067	1.676	.712	7.422
	Equal variances not assumed			2.426	53.223	.019	4.067	1.676	.705	7.428
PERIOP HEART RATE-AI	Equal variances assumed	1.817	.183	2.389	58	.020	3.733	1.563	.605	6.861
	Equal variances not assumed			2.389	54.891	.020	3.733	1.563	.602	6.865
PERIOP HEART RATE-5	Equal variances assumed	1.194	.279	2.927	58	.005	4.833	1.651	1.528	8.139
	Equal variances not assumed			2.927	56.847	.005	4.833	1.651	1.526	8.140
PERIOP HEART RATE-1(	Equal variances assumed	.369	.546	2.740	58	.008	4.767	1.740	1.284	8.249
	Equal variances not assumed			2.740	56.943	.008	4.767	1.740	1.282	8.251
PERIOP HEART RATE-1!	Equal variances assumed	.201	.656	2.028	58	.047	3.333	1.643	.044	6.623
	Equal variances not assumed			2.028	57.580	.047	3.333	1.643	.043	6.623
PERIOP HEART RATE-2(	Equal variances assumed	1.272	.264	2.316	58	.024	3.767	1.627	.510	7.023
	Equal variances not assumed			2.316	55.842	.024	3.767	1.627	.508	7.026
PERIOP HEART RATE-2!	Equal variances assumed	1.726	.194	2.161	58	.035	6.767	3.132	.498	13.035
	Equal variances not assumed			2.161	35.436	.038	6.767	3.132	.412	13.121
PERIOP HEART RATE-3(	Equal variances assumed	1.688	.199	2.512	58	.015	4.000	1.592	.813	7.187
	Equal variances not assumed			2.512	55.780	.015	4.000	1.592	.810	7.190
PERIOP HEART RATE-3!	Equal variances assumed	4.274	.043	2.289	58	.026	3.767	1.646	.472	7.061
	Equal variances not assumed			2.289	54.498	.026	3.767	1.646	.468	7.065
PERIOP HEART RATE-4(	Equal variances assumed	.575	.451	2.421	58	.019	3.700	1.528	.641	6.759
	Equal variances not assumed			2.421	57.561	.019	3.700	1.528	.640	6.760
PERIOP HEART RATE-4!	Equal variances assumed	1.985	.164	2.585	58	.012	7.800	3.017	1.761	13.839
	Equal variances not assumed			2.585	36.284	.014	7.800	3.017	1.683	13.917
PERIOP HEART RATE-1 hr	Equal variances assumed	1.707	.197	3.823	58	.000	6.033	1.578	2.874	9.192
	Equal variances not assumed			3.823	55.287	.000	6.033	1.578	2.871	9.196
PERIOP HEART RATE-2 hr	Equal variances assumed	2.318	.133	3.920	58	.000	5.967	1.522	2.920	9.014
	Equal variances not assumed			3.920	54.147	.000	5.967	1.522	2.915	9.018
PERIOP HEART RATE-3 hr	Equal variances assumed	1.367	.247	2.674	58	.010	4.333	1.621	1.089	7.577
	Equal variances not assumed			2.674	55.639	.010	4.333	1.621	1.086	7.580
PERIOP HEART RATE-4 hr	Equal variances assumed	.391	.534	2.353	58	.022	3.867	1.643	.578	7.156
	Equal variances not assumed			2.353	57.416	.022	3.867	1.643	.577	7.156
PERIOP HEART RATE-5 hr	Equal variances assumed	.005	.945	3.507	38	.001	8.333	2.376	3.523	13.144
	Equal variances not assumed			3.543	30.588	.001	8.333	2.352	3.534	13.133

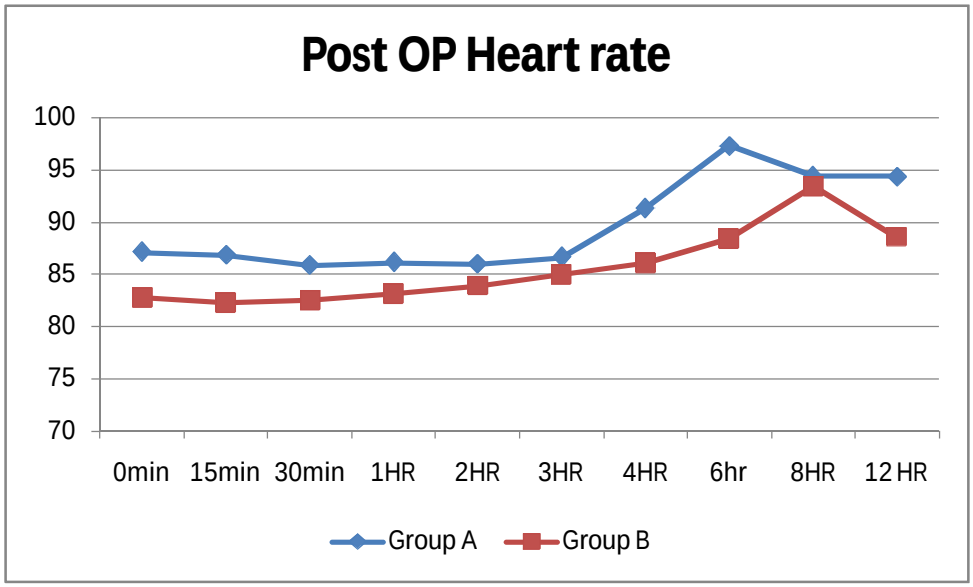


Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
POST OP HEARTRATE0	GROUP A	30	87.17	6.379	1.165
	GROUP B	30	82.80	6.277	1.146
POST OP HEARTRATE15	GROUP A	30	86.90	6.593	1.204
	GROUP B	30	82.27	6.158	1.124
POST OP HEARTRATE30	GROUP A	30	85.90	6.370	1.163
	GROUP B	30	82.57	6.240	1.139
POST OP HEARTRATE1HR	GROUP A	30	86.17	5.670	1.035
	GROUP B	30	83.13	6.585	1.202
POST OP HEARTRATE-2HR	GROUP A	30	86.00	5.608	1.024
	GROUP B	30	83.93	5.795	1.058
POST OP HEARTRATE-3HR	GROUP A	30	86.67	5.909	1.079
	GROUP B	30	85.00	5.687	1.038
POST OP HEARTRATE-4HR	GROUP A	30	91.37	6.483	1.184
	GROUP B	30	86.10	5.635	1.029
POST OP HEARTRATE-6hr	GROUP A	30	97.33	5.744	1.049
	GROUP B	30	88.47	5.104	.932
POST OP HEARTRATE-8HR	GROUP A	30	94.47	5.551	1.013
	GROUP B	30	93.50	6.766	1.235
POST OP HEARTRATE-12 HR	GROUP A	30	94.37	4.367	.797
	GROUP B	30	88.60	6.521	1.191

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
POST OP HEARTRATE0	Equal variances assumed	.662	.419	2.672	58	.010	4.367	1.634	1.096	7.638
	Equal variances not assumed			2.672	57.985	.010	4.367	1.634	1.096	7.638
POST OP HEARTRATE15	Equal variances assumed	.949	.334	2.813	58	.007	4.633	1.647	1.336	7.931
	Equal variances not assumed			2.813	57.732	.007	4.633	1.647	1.336	7.931
POST OP HEARTRATE30	Equal variances assumed	.160	.690	2.047	58	.045	3.333	1.628	.074	6.592
	Equal variances not assumed			2.047	57.976	.045	3.333	1.628	.074	6.592
POST OP HEARTRATE1HR	Equal variances assumed	.230	.633	1.912	58	.061	3.033	1.586	-.142	6.209
	Equal variances not assumed			1.912	56.748	.061	3.033	1.586	-.144	6.210
POST OP HEARTRATE-2HR	Equal variances assumed	.383	.539	1.404	58	.166	2.067	1.472	-.880	5.014
	Equal variances not assumed			1.404	57.938	.166	2.067	1.472	-.881	5.014
POST OP HEARTRATE-3HR	Equal variances assumed	.458	.501	1.113	58	.270	1.667	1.497	-1.331	4.664
	Equal variances not assumed			1.113	57.915	.270	1.667	1.497	-1.331	4.664
POST OP HEARTRATE-4HR	Equal variances assumed	.120	.730	3.358	58	.001	5.267	1.568	2.127	8.406
	Equal variances not assumed			3.358	56.894	.001	5.267	1.568	2.126	8.407
POST OP HEARTRATE-6hr	Equal variances assumed	.855	.359	6.320	58	.000	8.867	1.403	6.059	11.675
	Equal variances not assumed			6.320	57.210	.000	8.867	1.403	6.058	11.676
POST OP HEARTRATE-8HR	Equal variances assumed	.947	.335	.605	58	.548	.967	1.598	-2.232	4.165
	Equal variances not assumed			.605	55.866	.548	.967	1.598	-2.234	4.168
POST OP HEARTRATE-12 HR	Equal variances assumed	4.663	.035	4.025	58	.000	5.767	1.433	2.899	8.635
	Equal variances not assumed			4.025	50.653	.000	5.767	1.433	2.890	8.644

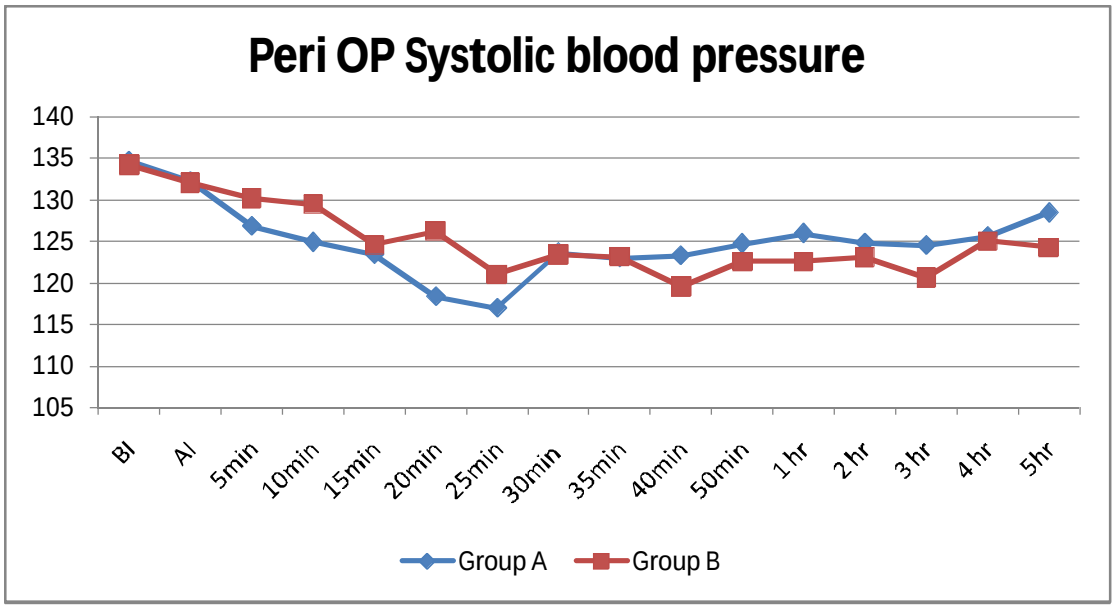


The heart rate of patients measure at different time points showed

statistically significant results in group A and group B.(P<0.05).

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
PERIOP SYSTOLIC BP-BI	GROUP A	30	134.70	5.547	1.013
	GROUP B	30	134.27	4.777	.872
PERIOP SYSTOLIC BP-AI	GROUP A	30	132.27	5.099	.931
	GROUP B	30	132.10	4.521	.825
PERIOP SYSTOLIC BP-5	GROUP A	30	126.90	20.246	3.696
	GROUP B	30	130.23	5.217	.953
PERIOP SYSTOLIC BP-10	GROUP A	30	124.93	17.281	3.155
	GROUP B	30	129.50	4.666	.852
PERIOP SYSTOLIC BP-15	GROUP A	30	123.40	17.352	3.168
	GROUP B	30	124.60	20.290	3.704
PERIOP SYSTOLIC BP-20	GROUP A	30	118.40	25.099	4.582
	GROUP B	30	126.27	4.961	.906
PERIOP SYSTOLIC BP-25	GROUP A	30	117.00	26.176	4.779
	GROUP B	30	121.03	20.147	3.678
PERIOP SYSTOLIC BP-30	GROUP A	30	123.67	5.460	.997
	GROUP B	30	123.40	4.687	.856
PERIOP SYSTOLIC BP-35	GROUP A	30	123.03	5.359	.978
	GROUP B	30	123.17	4.035	.737
PERIOP SYSTOLIC BP-40	GROUP A	30	123.33	4.326	.790
	GROUP B	30	119.53	18.424	3.364
PERIOP SYSTOLIC BP-45	GROUP A	30	124.50	5.204	.950
	GROUP B	30	122.60	4.523	.826
PERIOP SYSTOLIC BP-50	GROUP A	30	124.77	5.056	.923
	GROUP B	30	122.57	4.904	.895
PERIOP SYSTOLIC BP-1 hr	GROUP A	30	126.00	5.045	.921
	GROUP B	30	122.60	5.062	.924
PERIOP SYSTOLIC BP-2 hr	GROUP A	29	124.83	5.000	.929
	GROUP B	30	123.13	4.377	.799
PERIOP SYSTOLIC BP-3 hr	GROUP A	29	124.55	5.040	.936
	GROUP B	30	120.60	18.799	3.432
PERIOP SYSTOLIC BP-4 hr	GROUP A	28	125.64	6.384	1.206
	GROUP B	30	125.07	3.930	.717
PERIOP SYSTOLIC BP-5hr	GROUP A	23	128.48	8.628	1.799
	GROUP B	29	124.28	10.302	1.913

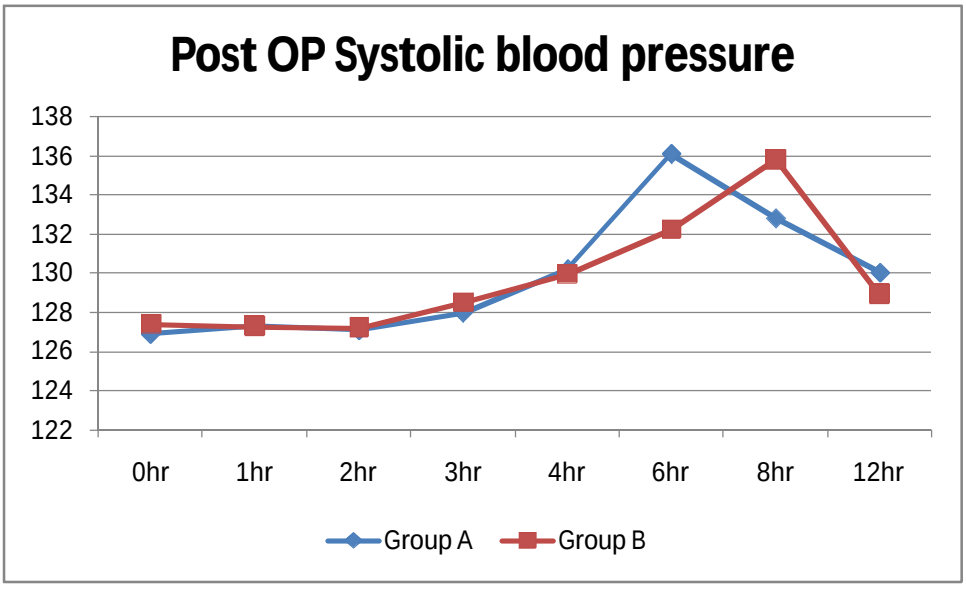


Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
PERIOP SYSTOLIC BP-BI	Equal variances assumed	1.825	.182	.324	58	.747	.433	1.337	-2.242	3.109
	Equal variances not assumed			.324	56.752	.747	.433	1.337	-2.243	3.110
PERIOP SYSTOLIC BP-AI	Equal variances assumed	2.650	.109	.134	58	.894	.167	1.244	-2.324	2.657
	Equal variances not assumed			.134	57.181	.894	.167	1.244	-2.324	2.658
PERIOP SYSTOLIC BP-5	Equal variances assumed	1.556	.217	-.873	58	.386	-3.333	3.817	-10.974	4.307
	Equal variances not assumed			-.873	32.835	.389	-3.333	3.817	-11.101	4.434
PERIOP SYSTOLIC BP-10	Equal variances assumed	1.744	.192	-1.397	58	.168	-4.567	3.268	-11.108	1.975
	Equal variances not assumed			-1.397	33.207	.172	-4.567	3.268	-11.214	2.081
PERIOP SYSTOLIC BP-15	Equal variances assumed	.025	.875	-.246	58	.806	-1.200	4.874	-10.957	8.557
	Equal variances not assumed			-.246	56.636	.806	-1.200	4.874	-10.962	8.562
PERIOP SYSTOLIC BP-20	Equal variances assumed	4.674	.035	-1.684	58	.098	-7.867	4.671	-17.217	1.484
	Equal variances not assumed			-1.684	31.263	.102	-7.867	4.671	-17.390	1.657
PERIOP SYSTOLIC BP-25	Equal variances assumed	.752	.389	-.669	58	.506	-4.033	6.031	-16.105	8.038
	Equal variances not assumed			-.669	54.434	.506	-4.033	6.031	-16.122	8.055
PERIOP SYSTOLIC BP-30	Equal variances assumed	2.251	.139	.203	58	.840	.267	1.314	-2.363	2.897
	Equal variances not assumed			.203	56.699	.840	.267	1.314	-2.365	2.898
PERIOP SYSTOLIC BP-35	Equal variances assumed	1.433	.236	-.109	58	.914	-.133	1.225	-2.585	2.318
	Equal variances not assumed			-.109	53.882	.914	-.133	1.225	-2.589	2.322
PERIOP SYSTOLIC BP-40	Equal variances assumed	1.450	.233	1.100	58	.276	3.800	3.455	-3.116	10.716
	Equal variances not assumed			1.100	32.188	.280	3.800	3.455	-3.236	10.836
PERIOP SYSTOLIC BP-45	Equal variances assumed	.028	.867	1.509	58	.137	1.900	1.259	-.620	4.420
	Equal variances not assumed			1.509	56.893	.137	1.900	1.259	-.621	4.421
PERIOP SYSTOLIC BP-50	Equal variances assumed	.058	.810	1.711	58	.092	2.200	1.286	-.374	4.774
	Equal variances not assumed			1.711	57.946	.092	2.200	1.286	-.374	4.774
PERIOP SYSTOLIC BP-1 hr	Equal variances assumed	.000	.986	2.606	58	.012	3.400	1.305	.788	6.012
	Equal variances not assumed			2.606	57.999	.012	3.400	1.305	.788	6.012
PERIOP SYSTOLIC BP-2 hr	Equal variances assumed	.368	.547	1.386	57	.171	1.694	1.222	-.753	4.142
	Equal variances not assumed			1.383	55.459	.172	1.694	1.225	-.760	4.149
PERIOP SYSTOLIC BP-3 hr	Equal variances assumed	1.364	.248	1.094	57	.278	3.952	3.611	-3.279	11.183
	Equal variances not assumed			1.111	33.282	.275	3.952	3.558	-3.284	11.187
PERIOP SYSTOLIC BP-4 hr	Equal variances assumed	3.821	.056	.417	56	.678	.576	1.382	-2.192	3.344
	Equal variances not assumed			.410	44.314	.683	.576	1.404	-2.252	3.405
PERIOP SYSTOLIC BP-5hr	Equal variances assumed	.527	.471	1.568	50	.123	4.202	2.681	-1.182	9.587
	Equal variances not assumed			1.600	49.826	.116	4.202	2.626	-1.073	9.478

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
POST OP SYSTOLIC BP-(	GROUP A	30	126.93	5.663	1.034
	GROUP B	30	127.37	4.560	.833
POST OP SYSTOLIC BP-1	GROUP A	30	127.33	4.505	.823
	GROUP B	30	127.27	4.283	.782
POST OP SYSTOLIC BP-2	GROUP A	30	127.10	5.095	.930
	GROUP B	30	127.20	4.221	.771
POST OP SYSTOLIC BP-3	GROUP A	30	128.00	5.350	.977
	GROUP B	30	128.50	4.652	.849
POST OP SYSTOLIC BP-4	GROUP A	30	130.20	5.365	.980
	GROUP B	30	129.93	4.806	.877
POST OP SYSTOLIC BP-(	GROUP A	30	136.10	5.962	1.088
	GROUP B	30	132.23	5.544	1.012
POST OP SYSTOLIC BP-8	GROUP A	30	132.83	5.748	1.049
	GROUP B	30	135.83	5.370	.980
POST OP SYSTOLIC BP-1	GROUP A	22	130.05	6.492	1.384
	GROUP B	30	128.93	18.122	3.309



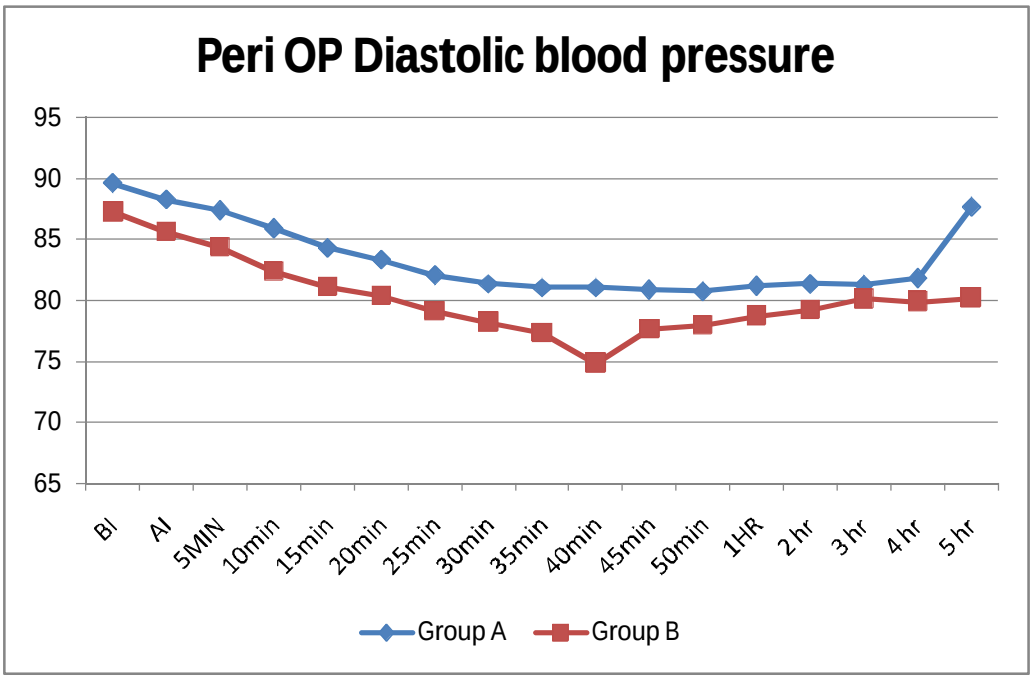
Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
POST OP SYSTOLIC BP-0	Equal variances assumed	1.340	.252	-.326	58	.745	-.433	1.327	-3.090	2.224
	Equal variances not assumed			-.326	55.477	.745	-.433	1.327	-3.093	2.226
POST OP SYSTOLIC BP-1	Equal variances assumed	.000	.989	.059	58	.953	.067	1.135	-2.205	2.338
	Equal variances not assumed			.059	57.851	.953	.067	1.135	-2.205	2.339
POST OP SYSTOLIC BP-2	Equal variances assumed	1.116	.295	-.083	58	.934	-.100	1.208	-2.518	2.318
	Equal variances not assumed			-.083	56.064	.934	-.100	1.208	-2.520	2.320
POST OP SYSTOLIC BP-3	Equal variances assumed	1.065	.306	-.386	58	.701	-.500	1.294	-3.091	2.091
	Equal variances not assumed			-.386	56.902	.701	-.500	1.294	-3.092	2.092
POST OP SYSTOLIC BP-4	Equal variances assumed	1.798	.185	.203	58	.840	.267	1.315	-2.366	2.899
	Equal variances not assumed			.203	57.311	.840	.267	1.315	-2.366	2.900
POST OP SYSTOLIC BP-6	Equal variances assumed	1.184	.281	2.601	58	.012	3.867	1.486	.891	6.842
	Equal variances not assumed			2.601	57.697	.012	3.867	1.486	.891	6.842
POST OP SYSTOLIC BP-8	Equal variances assumed	.157	.693	-2.089	58	.041	-3.000	1.436	-5.875	-.125
	Equal variances not assumed			-2.089	57.733	.041	-3.000	1.436	-5.875	-.125
POST OP SYSTOLIC BP-12	Equal variances assumed	.486	.489	.275	50	.785	1.112	4.050	-7.022	9.247
	Equal variances not assumed			.310	38.413	.758	1.112	3.586	-6.146	8.370

The systolic pressure measured at different points beween two groups showed statistical significance at three points.(P<0.05).

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
PERI OP DIASTOLIC BP-BI	GROUP A	30	89.63	4.351	.794
	GROUP B	30	87.30	4.822	.880
PERI OP DIASTOLIC BP-AI	GROUP A	30	88.30	4.786	.874
	GROUP B	30	85.63	4.567	.834
PERI OP DIASTOLIC BP-5	GROUP A	30	87.40	4.430	.809
	GROUP B	30	84.37	4.895	.894
PERI OP DIASTOLIC BP-10	GROUP A	30	85.93	4.961	.906
	GROUP B	30	82.40	5.008	.914
PERI OP DIASTOLIC BP-15	GROUP A	30	84.33	5.561	1.015
	GROUP B	30	81.10	4.444	.811
PERI OP DIASTOLIC BP-20	GROUP A	30	83.37	4.824	.881
	GROUP B	30	80.37	4.537	.828
PERI OP DIASTOLIC BP-25	GROUP A	30	82.10	5.326	.972
	GROUP B	30	79.13	4.674	.853
PERI OP DIASTOLIC BP-30	GROUP A	30	81.40	4.149	.757
	GROUP B	30	78.23	4.847	.885
PERI OP DIASTOLIC BP-35	GROUP A	30	81.10	3.726	.680
	GROUP B	29	77.34	5.080	.943
PERI OP DIASTOLIC BP-40	GROUP A	30	81.10	3.315	.605
	GROUP B	30	74.83	13.757	2.512
PERI OP DIASTOLIC BP-45	GROUP A	30	80.93	4.068	.743
	GROUP B	30	77.67	4.852	.886
PERI OP DIASTOLIC BP-50	GROUP A	30	80.80	4.147	.757
	GROUP B	30	77.97	4.944	.903
PERI OP DIASTOLIC BP-1HR	GROUP A	30	81.23	5.104	.932
	GROUP B	30	78.73	5.219	.953
PERI OP DIASTOLIC BP-2 hr	GROUP A	29	81.38	4.570	.849
	GROUP B	30	79.20	5.404	.987
PERI OP DIASTOLIC BP-3 hr	GROUP A	29	81.31	4.481	.832
	GROUP B	30	80.13	5.680	1.037
PERI OP DIASTOLIC BP-4 hr	GROUP A	28	81.86	4.972	.940
	GROUP B	30	79.90	5.827	1.064
PERI OP DIASTOLIC BP-5 hr	GROUP A	17	87.71	7.622	1.849
	GROUP B	27	80.22	6.009	1.156



Independent Samples Test

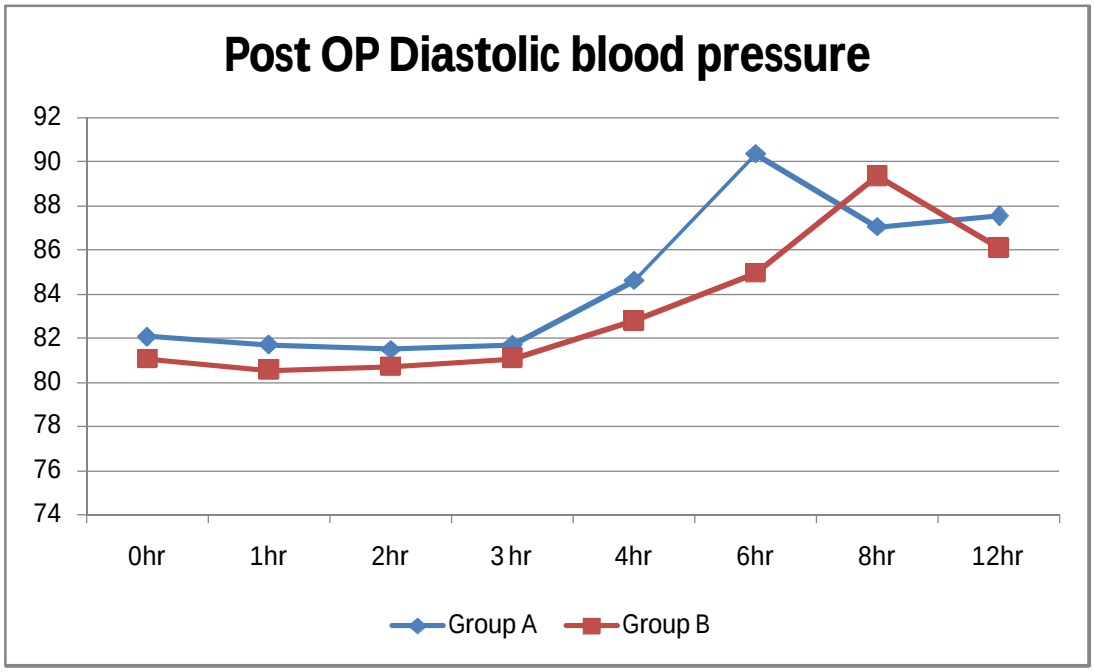
		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
PERI OP DIASTOLIC BP-BI	Equal variances assumed	.277	.601	1.968	58	.054	2.333	1.186	-.040	4.707
	Equal variances not assumed			1.968	57.397	.054	2.333	1.186	-.041	4.707
PERI OP DIASTOLIC BP-AI	Equal variances assumed	.002	.966	2.208	58	.031	2.667	1.208	.249	5.084
	Equal variances not assumed			2.208	57.874	.031	2.667	1.208	.249	5.085
PERI OP DIASTOLIC BP-5	Equal variances assumed	.011	.919	2.516	58	.015	3.033	1.205	.620	5.446
	Equal variances not assumed			2.516	57.432	.015	3.033	1.205	.620	5.447
PERI OP DIASTOLIC BP-10	Equal variances assumed	.098	.756	2.745	58	.008	3.533	1.287	.957	6.110
	Equal variances not assumed			2.745	57.995	.008	3.533	1.287	.957	6.110
PERI OP DIASTOLIC BP-15	Equal variances assumed	1.446	.234	2.488	58	.016	3.233	1.300	.632	5.835
	Equal variances not assumed			2.488	55.311	.016	3.233	1.300	.629	5.837
PERI OP DIASTOLIC BP-20	Equal variances assumed	.923	.341	2.481	58	.016	3.000	1.209	.580	5.420
	Equal variances not assumed			2.481	57.783	.016	3.000	1.209	.579	5.421
PERI OP DIASTOLIC BP-25	Equal variances assumed	.954	.333	2.293	58	.025	2.967	1.294	.377	5.556
	Equal variances not assumed			2.293	57.037	.026	2.967	1.294	.376	5.557
PERI OP DIASTOLIC BP-30	Equal variances assumed	.146	.704	2.718	58	.009	3.167	1.165	.835	5.498
	Equal variances not assumed			2.718	56.651	.009	3.167	1.165	.834	5.500
PERI OP DIASTOLIC BP-35	Equal variances assumed	1.305	.258	3.245	57	.002	3.755	1.157	1.438	6.072
	Equal variances not assumed			3.229	51.303	.002	3.755	1.163	1.421	6.090
PERI OP DIASTOLIC BP-40	Equal variances assumed	2.341	.131	2.426	58	.018	6.267	2.584	1.095	11.438
	Equal variances not assumed			2.426	32.357	.021	6.267	2.584	1.006	11.527
PERI OP DIASTOLIC BP-45	Equal variances assumed	.066	.798	2.826	58	.006	3.267	1.156	.953	5.581
	Equal variances not assumed			2.826	56.287	.007	3.267	1.156	.951	5.582
PERI OP DIASTOLIC BP-50	Equal variances assumed	.643	.426	2.405	58	.019	2.833	1.178	.475	5.192
	Equal variances not assumed			2.405	56.295	.019	2.833	1.178	.473	5.193
PERI OP DIASTOLIC BP-1HR	Equal variances assumed	.016	.900	1.876	58	.066	2.500	1.333	-.168	5.168
	Equal variances not assumed			1.876	57.971	.066	2.500	1.333	-.168	5.168
PERI OP DIASTOLIC BP-2 hr	Equal variances assumed	.696	.407	1.670	57	.100	2.179	1.305	-.434	4.793
	Equal variances not assumed			1.675	56.025	.100	2.179	1.301	-.428	4.786
PERI OP DIASTOLIC BP-3 hr	Equal variances assumed	2.884	.095	.882	57	.382	1.177	1.335	-1.496	3.850
	Equal variances not assumed			.885	54.827	.380	1.177	1.330	-1.488	3.842
PERI OP DIASTOLIC BP-4 hr	Equal variances assumed	.464	.499	1.371	56	.176	1.957	1.427	-.902	4.816
	Equal variances not assumed			1.379	55.570	.173	1.957	1.419	-.887	4.801
PERI OP DIASTOLIC BP-5 hr	Equal variances assumed	2.062	.158	3.624	42	.001	7.484	2.065	3.316	11.651
	Equal variances not assumed			3.432	28.304	.002	7.484	2.180	3.019	11.948

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
POST OP DIASTOLIC BP -0	GROUP A	30	82.10	6.155	1.124
	GROUP B	30	81.07	4.941	.902
POST OP DIASTOLIC BP -1	GROUP A	30	81.73	5.860	1.070
	GROUP B	30	80.57	4.500	.822
POST OP DIASTOLIC BP -2	GROUP A	30	81.53	5.877	1.073
	GROUP B	30	80.73	4.283	.782
POST OP DIASTOLIC BP -3	GROUP A	30	81.73	5.265	.961
	GROUP B	30	81.10	4.188	.765
POST OP DIASTOLIC BP -4	GROUP A	30	84.63	5.116	.934
	GROUP B	30	82.80	4.679	.854
POST OP DIASTOLIC BP -6	GROUP A	30	90.37	5.000	.913
	GROUP B	30	84.97	4.796	.876
POST OP DIASTOLIC BP -8	GROUP A	30	87.07	4.877	.890
	GROUP B	30	89.37	4.965	.907
POST OP DIASTOLIC BP -12	GROUP A	28	87.57	5.266	.995
	GROUP B	30	86.10	5.714	1.043

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
POST OP DIASTOLIC BP -0	Equal variances assumed	2.887	.095	.717	58	.476	1.033	1.441	-1.851	3.918
	Equal variances not assumed			.717	55.407	.476	1.033	1.441	-1.854	3.921
POST OP DIASTOLIC BP -1	Equal variances assumed	2.526	.117	.865	58	.391	1.167	1.349	-1.534	3.867
	Equal variances not assumed			.865	54.380	.391	1.167	1.349	-1.537	3.871
POST OP DIASTOLIC BP -2	Equal variances assumed	6.321	.015	.603	58	.549	.800	1.328	-1.857	3.457
	Equal variances not assumed			.603	53.026	.549	.800	1.328	-1.863	3.463
POST OP DIASTOLIC BP -3	Equal variances assumed	3.323	.073	.516	58	.608	.633	1.228	-1.825	3.092
	Equal variances not assumed			.516	55.208	.608	.633	1.228	-1.828	3.095
POST OP DIASTOLIC BP -4	Equal variances assumed	.270	.606	1.448	58	.153	1.833	1.266	-.700	4.367
	Equal variances not assumed			1.448	57.543	.153	1.833	1.266	-.701	4.367
POST OP DIASTOLIC BP -6	Equal variances assumed	.856	.359	4.269	58	.000	5.400	1.265	2.868	7.932
	Equal variances not assumed			4.269	57.899	.000	5.400	1.265	2.868	7.932
POST OP DIASTOLIC BP -8	Equal variances assumed	.025	.876	-1.810	58	.075	-2.300	1.271	-4.844	.244
	Equal variances not assumed			-1.810	57.981	.075	-2.300	1.271	-4.844	.244
POST OP DIASTOLIC BP -1	Equal variances assumed	.337	.564	1.018	56	.313	1.471	1.446	-1.425	4.368
	Equal variances not assumed			1.021	55.993	.312	1.471	1.442	-1.417	4.360



The diastolic blood pressure compared between two groups at different points are statistically significant.(P<0.05).

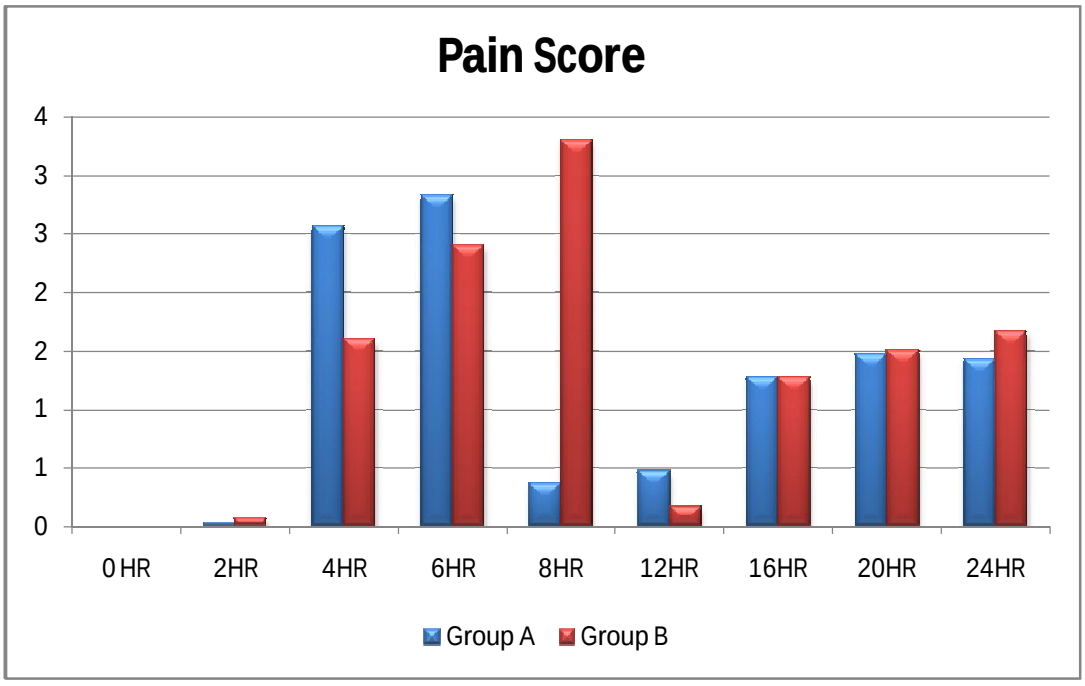
Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
PAIN SCORE - 0HR	GROUP A	30	.00	.000[a]	.000
	GROUP B	30	.00	.000[a]	.000
PAIN SCORE - 2HR	GROUP A	30	.03	.183	.033
	GROUP B	30	.07	.254	.046
PAIN SCORE - 4HR	GROUP A	30	2.57	.935	.171
	GROUP B	30	1.60	.621	.113
PAIN SCORE - 6HR	GROUP A	30	2.83	1.663	.304
	GROUP B	30	2.40	.932	.170
PAIN SCORE - 8HR	GROUP A	30	.37	1.066	.195
	GROUP B	30	3.30	1.512	.276
PAIN SCORE - 12HR	GROUP A	30	.47	.629	.115
	GROUP B	30	.17	.379	.069
PAIN SCORE - 16HR	GROUP A	30	1.27	.450	.082
	GROUP B	30	1.27	.521	.095
PAIN SCORE - 20HR	GROUP A	30	1.47	.571	.104
	GROUP B	30	1.50	.572	.104
PAIN SCORE - 24HR	GROUP A	30	1.43	.679	.124
	GROUP B	30	1.67	.479	.088

a. t cannot be computed because the standard deviations of both groups are 0.

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
PAIN SCORE - 2HR	Equal variances assumed	1.396	.242	-.584	58	.561	-.033	.057	-.148	.081
	Equal variances not assumed			-.584	52.684	.562	-.033	.057	-.148	.081
PAIN SCORE - 4HR	Equal variances assumed	7.061	.010	4.715	58	.000	.967	.205	.556	1.377
	Equal variances not assumed			4.715	50.431	.000	.967	.205	.555	1.378
PAIN SCORE - 6HR	Equal variances assumed	10.429	.002	1.245	58	.218	.433	.348	-.263	1.130
	Equal variances not assumed			1.245	45.592	.219	.433	.348	-.267	1.134
PAIN SCORE - 8HR	Equal variances assumed	4.123	.047	-8.684	58	.000	-2.933	.338	-3.609	-2.257
	Equal variances not assumed			-8.684	52.123	.000	-2.933	.338	-3.611	-2.256
PAIN SCORE - 12HR	Equal variances assumed	17.720	.000	2.238	58	.029	.300	.134	.032	.568
	Equal variances not assumed			2.238	47.617	.030	.300	.134	.030	.570
PAIN SCORE - 16HR	Equal variances assumed	.623	.433	.000	58	1.000	.000	.126	-.251	.251
	Equal variances not assumed			.000	56.795	1.000	.000	.126	-.252	.252
PAIN SCORE - 20HR	Equal variances assumed	.008	.927	-.226	58	.822	-.033	.148	-.329	.262
	Equal variances not assumed			-.226	58.000	.822	-.033	.148	-.329	.262
PAIN SCORE - 24HR	Equal variances assumed	5.730	.020	-1.538	58	.130	-.233	.152	-.537	.070
	Equal variances not assumed			-1.538	52.165	.130	-.233	.152	-.538	.071



Mann-Whitney Test

Ranks

	GROUP	N	Mean Rank	Sum of Ranks
PAIN SCORE - 0HR	GROUP A	30	30.50	915.00
	GROUP B	30	30.50	915.00
	Total	60		
PAIN SCORE - 2HR	GROUP A	30	30.00	900.00
	GROUP B	30	31.00	930.00
	Total	60		
PAIN SCORE - 4HR	GROUP A	30	38.90	1167.00
	GROUP B	30	22.10	663.00
	Total	60		
PAIN SCORE - 6HR	GROUP A	30	35.13	1054.00
	GROUP B	30	25.87	776.00
	Total	60		
PAIN SCORE - 8HR	GROUP A	30	19.20	576.00
	GROUP B	30	41.80	1254.00
	Total	60		
PAIN SCORE - 12HR	GROUP A	30	34.17	1025.00
	GROUP B	30	26.83	805.00
	Total	60		
PAIN SCORE - 16HR	GROUP A	30	30.37	911.00
	GROUP B	30	30.63	919.00
	Total	60		
PAIN SCORE - 20HR	GROUP A	30	30.02	900.50
	GROUP B	30	30.98	929.50
	Total	60		
PAIN SCORE - 24HR	GROUP A	30	27.50	825.00
	GROUP B	30	33.50	1005.00
	Total	60		

Test Statistics

	AIN SCOR - 0HR	AIN SCOR - 2HR	AIN SCOR - 4HR	AIN SCOR - 6HR	AIN SCOR - 8HR	AIN SCOR - 12HR	AIN SCOR - 16HR	AIN SCOR - 20HR	AIN SCOR - 24HR
Mann-Whitney	450.000	435.000	198.000	311.000	111.000	340.000	446.000	435.500	360.000
Wilcoxon W	915.000	900.000	663.000	776.000	576.000	805.000	911.000	900.500	825.000
Z	.000	-.587	-4.022	-2.138	-5.672	-2.071	-.074	-.246	-1.517
Asymp. Sig. (2	1.000	.557	.000	.033	.000	.038	.941	.806	.129

a. Grouping Variable: GROUP

In this study the quality of analgesia in group A and B were compared using visual analog scale. This parameter is statistically significant ($P<0.05$) in both the groups.

DISCUSSION

This randomized,prospective,blinded study has been done to compare the analgesic efficacy of 0.25% Bupivacaine with 10mg nalbuphine and 0.25% Bupivacaine with 50mg tramadol administered epidurally.

1. The total duration of sensory analgesia was 300+/- 11.493 among patients in group A and in group was 320+/- 9.80minutes.The total duration of postoperative analgesia in patients in group B was prolonged as compared to group A but found to be statistically insignificant. This result is comparable with veena chatrath et al.
2. In this study with use of 0.25% Bupivacaine with nalbuphine and 0.25% Bupivacaine with tramadol administered epidurally,the mean number of top up doses given in group A as 5.08 +/- 0.694,as compared to 4.90 +/- 0.900 in group B and the difference between the two groups was found to be statistically insignificant.These results are comparable with gunion et al.
3. The mean systolic blood pressures and diastolic blood pressures have been found to be statistically significant ($P<0.05$) in both the groups.According to Grass JA (1998), wheatley RG,Schug SA,Watson D(2001) strategies to prevent non critical hypotension was to decrease the overall dose of local anaesthetic or decrease the concentration of local anaesthetic.

Most evidence indicates that Fentanyl produces little or no change in myocardial contractility but has positive inotropic effect. Possible mechanisms of positive inottropic effect. possible mechanisms of positive

inotropic effects of fentanyl include catecholamine release or direct myocardial adrenergic activation. According to William F Ganong (1995) pain usually causes rise in blood pressure via afferent impulses in the reticular formation converging on the vasomotor area , a group of neurons in medulla oblongata that mainly control blood pressure. Opiods also can modulate the stress response through receptor mediated actions on the hypothalamic-pituitary-adrenal axis.

In this study rise in blood pressures were seen in group A and B ,when the effect of bolus dose weaned off and Visual Analog Scales increased.

4. The mean heart rate which has been found to be statistically significant in both the groups. Murat et al(1988) observed that carotid sinus baroceptor reflex control of heart rate is markedly depressed by fentanyl at a rate of 10mcg/kg administered to neonates. In our study lo dose fentanyl was used to provide analgesia. The rise in heart rate due to pain occurred in group A when the drug effect weaned where as in group B it was significantly maintained. Impulses like pain reaching the medulla affect the heart rate.The stimuli that increases the heart rate increases blood pressure.
5. The quality of analgesia as compared using visual analog scale has been found to be statistically significant ($P<0.05$) in group A and B.The significance was high in group B when compared with group A.This result is comparable with veena chatrath et al.

COMPLICATIONS DURING THE STUDY

In this study we did not observe any case characterizing respiratory depression in either group A or group B .This parameter was assessed using pulse oximetry, respiratory rate and level consciousness. Our results are comparable with those of Badner NH, Bandari R,Komar WE(1994).According to Bailey et al ,(1993) Pulse oximetry reliably detects opiod induced arterial hypoxemia.

Chaney (1995) suggested that the most reliable sign of depression of ventilation appeared to be depressed level of consciousness caused by Hypercarbia. Lam A M and Knil R L(1983) demonstrated that epidural Fentanyl does not cause delayed respiratory depression.

Gustaffsson et al (1992) described that the late respiratory depression following epidural opioids were seen mostly in older, poor risk patients with acute or chronic respiratory insufficiency and cases associated with excessive blood loss.

There were no cases characterizing opioid induced pruritis were observed. This result was comparable with those of Badner NH, Bandari R,Komar WE(1994).

12 patients among the group B had nausea,vomiting. This was treated with injection ondansetron (75mcg/kg).No patients among group A had nausea and vomiting.

In our study no cases had urinary retention among group A or group B.

CONCLUSION

We conclude that both nalbuphine and tramadol were effective for postoperative analgesia when used epidurally in patients undergoing lower limb revascularization surgeries. The nalbuphine group had better quality of surgical anaesthesia and lesser incidence of complications like nausea and vomiting. Also patient satisfaction was better among the nalbuphine group.

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PROFORMA

Date: Roll no:

Name: Age: Ht: Wt: Sex:

Diagnosis:

Surgical procedure:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

EXAMINATION: CVS: Hb : RS :

MEASURES OF STUDY OUTCOME:

HR SBP DBP SPO2 RR VAS

PRE OP

AFTER

SUB-ARACHNOID BLOCK

AFTER EPIDURAL TOP UP

15 MIN:

30 MIN

45 MIN :

60 MIN:

DOSE OF OPIOID USED FOR RESCUE ANALGESIA:

COMPLICATIONS IN INTRA OPERATIVE PERIOD:

POST OPERATIVE PAIN SCORE:

(Assessed every 30 minutes for first 24hrs post op)

INFORMATION TO PARTICIPANTS

Investigator:

Name of the Participant:

Title:

"Comparative Evaluation of Bupivacaine with Nalbuphine versus Bupivacaine with Tramadol for post operative analgesia in lower limb revascularization surgeries under combined spinal epidural anaesthesia ".

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria. We want to compare and study the safety and analgesic efficacy of epidural bupivacaine with nalbuhine versus epidural bupivacaine with tramadol for post operative analgesia in patients undergoing lower limb revascularization surgeries.

What is the Purpose of the Research:

This study is done to compare epidural bupivacaine with nalbuphine versus bupivacaine with tramadol bolus in patients undergoing lower limb revascularisation procedures with respect to

- Post-operative VAS score
- Intra-operative and post operative hemodynamics.

The Study Design:

All the patients in the study will be divided into two groups.

GROUP A : 0.5% of 2.5 ml bupivacaine intrathecally.Epidurally 0.25% bupivacaine(8ml) along with 10mg nalbuphine(2 ml) when sensory regression to T_{10}.

GROUP B : 0.5% of 2.5 ml bupivacaine intrathecally and epidurally 0.25% bupivacaine along with 50mg tramadol when sensory regression to T_{10}.

Benefits

Good pain relief intra operatively and post operatively.

Maintenance of intra operative and post operative hemodynamics.

Reduces the opioid requirement post operatively.

Discomforts and risks

Discomfort during block- this will be reduced by local infiltration.

Hypotension, bradycardia, nausea, vomiting, respiratory depression, sedation may occur – emergency drugs are readily available.

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative setting of standard treatment and your safety is our prime concern.

Time :

Date :

Place :

Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு :

கால் பகுதியிலுள்ள இரத்தகுழாய் மாற்று அறுவை சிகிச்சைக்கு கம்பைண்ட் ஸ்பெயினில் எப்பிடியூரல் முறையில் நால்பியூப்பைன் அல்லது டிரமடால் மருந்தினை பியூப்பிவேகெய்ன் மருந்தோடு கலவையாக்கி செலுத்தி வலியின்மையை ஒப்பிடுதல்.

ஆராய்ச்சி நிலையம் : இரத்தநாள அறுவை சிகிச்சைத்துறை,
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை மற்றும்
சென்னை மருத்துவக் கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் : உறவுமுறை :
பங்கு பெறுபவரின் எண். :

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்ஆய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்ஆய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம்..... இடம்..... தேதி
கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம்..... இடம்..... தேதி

ஆய்வாளரின் பெயர்.....

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சியாளர் பெயர் :

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சி தலைப்பு :

கால் பகுதியிலுள்ள இரத்தகுழாய் மாற்று அறுவை சிகிச்சைக்கு கம்பைண்ட் ஸ்பெயினில் எப்பிடியூரல் முறையில் நால்பியூப்பைன் அல்லது டிரமடால் மருந்தினை பியூப்பிவேகெய்ன் மருந்தோடு கலவையாக்கி செலுத்தி வலியின்மையை ஒப்பிடுதல்.

ஆராய்ச்சியின் நோக்கம்:

கால் பகுதியிலுள்ள இரத்தகுழாய் மாற்று அறுவை சிகிச்சைக்கு கம்பைண்ட் ஸ்பெயினில் எப்பிடியூரல் பகுதியினுள் நால்வியூப்பைன் அல்லது டிரமடால்மருந்தினை பியூப்பிவேகெய்ன் மருந்தோடு கலவையாக்கி செலுத்தி வலியின்மையை ஒப்பிடுதலே இந்த ஆய்வின் நோக்கமாகும்.

1) மேலே குறிப்பிட்டள்ள மருந்துகளின் மறத்துப்போகும் தன்மை அவகாசத்தை ஒப்பிடுதல்.
2) அறுவை சிகிச்கைக்குப்பின் இரத்த அழுத்தம் மற்றும் நாடித்துடிப்பு மாற்றங்கள்.
3) அறுவை சிகிச்சைக்குப் பிந்தைய வலி நிவாரணம் அளவு (விசுவல் அனலாக் அளவுகோல்)

ஆய்வின் தன்மை:

பங்கு பெறும் நோயாளிகள் இரண்டு குழுக்களாகப் பிரிக்கப்படுவர்.

குழு 1 : 0.5% 2.5 மி.லி. அளவு பியூப்பிவேகெய்ன் ஸ்பெயினல் பகுதியில் செலுத்தப்படும். T10 பகுதியில் வலி எப்பொழுது ஏற்படுகிறதோ அப்போது 0.25% பியூப்பிவேகெய்ன் (8 மி.லி), நால்பியூப்பைன் (10மி.லி), எப்பிடியூரல் பகுதியில் செலுத்தப்படும்.

குழு 2 : 0.5% 2.5 மி.லி. அளவு பியூப்பிவேகெய்ன் ஸ்பெயினல் பகுதியில் செலுத்தப்படும். T10 பகுதியில் வலி எப்பொழுது ஏற்படுகிறதோ அப்போது 0.25% பியூப்பிவேகெய்ன் (8 மி.லி), டிரமடால் 50mg (2மி.லி), எப்பிடியூரல் பகுதியில் செலுத்தப்படும்.

நன்மைகள்:

1. அறுவை சிகிச்சையின் போது நாடித்துடிப்பு மற்றும் இரத்த அழுத்தம் சீராக செயல்பட உதவுகின்றன.
2. இதர வலி நிவாரணிகளின் தேவை வெகுவாக குறைக்கப்படுகின்றன.
3. அறுவை சிகிச்சைக்குப் பின்னர் வலி நிவாரணத்தின் தன்மை நீட்டிக்கப்படுகின்றது.

ஏற்படும் உபாதைகள்:

ஊசி போடும் போது சௌகரியம் ஏற்படலாம். மரத்துப்போகும் ஊசியின் மூலம் இது தவிர்க்கப்படும். குறைந்த இரத்த அழுத்தம், குறைந்த நாடித்துடிப்பு ஏற்படலாம், வாந்தி, குமட்டல், அசதி மற்றும் மூச்சு விடுவதில் சீரற்ற தன்மை ஏற்படலாம். அதற்கு மாற்று மருந்துகள் உடனடியாகக் கொடுக்கப்படும்.

இந்த முறையான ஆய்வு ஏற்கனவே பல இடங்களில் நடத்தப்பட்டுள்ளது. மேலும் இதன் பாதுகாப்பு உறுதிசெய்யப்பட்டுள்ளது. நீங்கள் இந்த ஆய்வில் பங்குகொள்ள விரும்பவில்லை என்றால் எப்போதும் உபயோகிக்கப்படும் மருந்தே கொடுக்கப்படும். உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

இந்த ஆய்வு சம்பந்தமாக எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட் எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

ஆய்வாளரின் பெயர் பங்குகொள்பவரின் பெயர்

ஆய்வாளரின் கையொப்பம் பங்குபெறுபவரின் கையொப்பம்

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CERTIFICATE OF APPROVAL

To
Dr.Suganya.B.
II Year Post Graduate in M.D.(Anaesthesiology)
Madras Medical College & RGGGH
Chennai 600 003

Dear Dr.Suganya.B,

The Institutional Ethics Committee has considered your request and approved your study titled **"COMPARATIVE EVALUATION OF BUPIVACAINE WITH NALBUPHINE VERUS BUPIVACAINE WITH TRAMADOL FOR POST OPERATIVE ANALGESIA IN ELECTIVE LOWER LIMB REVASCULARIZATION SURGERIES UNDER COMBINED SPINAL EPIDURAL ANAESTHESIA " - NO.29032016.**

The following members of Ethics Committee were present in the meeting hold on **01.03.2016** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr.R.Vimala,MD.,Dean,MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.B.Vasanthi,MD.,Inst.of Pharmacology,MMC,Ch-3	: Member
5.Prof.P.Raghumani,MS, Dept.of Surgery,RGGGH,Ch-3	: Member
6.Dr.Baby Vasumathi, Director, Inst. of O&G,Ch-8	: Member
7.Prof.M.Saraswathi,MD.,Director, Inst.of Path,MMC,Ch-3	: Member
8.Prof.Srinivasagalu,Director,Inst.of Int.Med.,MMC,Ch-3	: Member
9.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
10.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
11.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

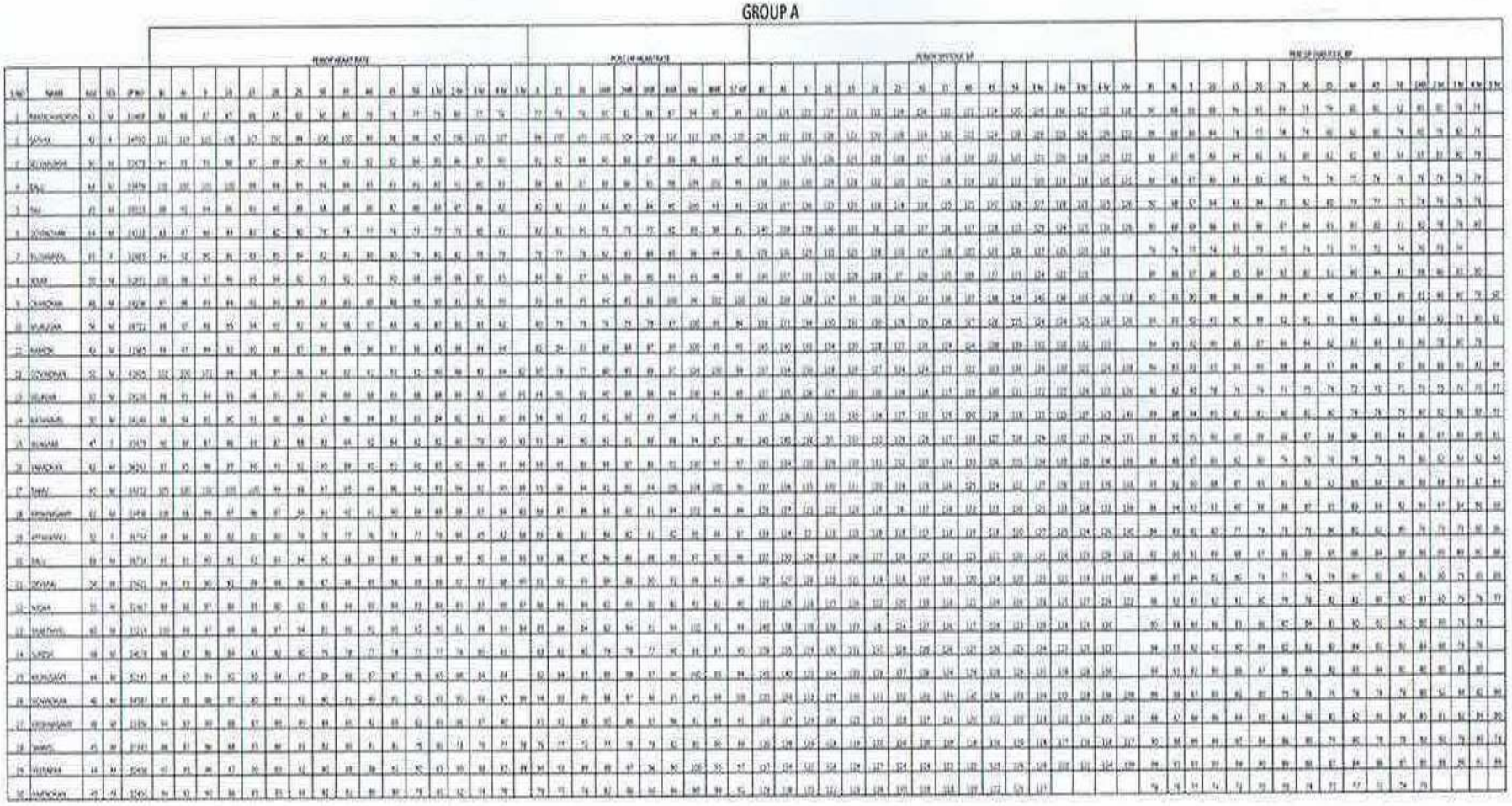
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

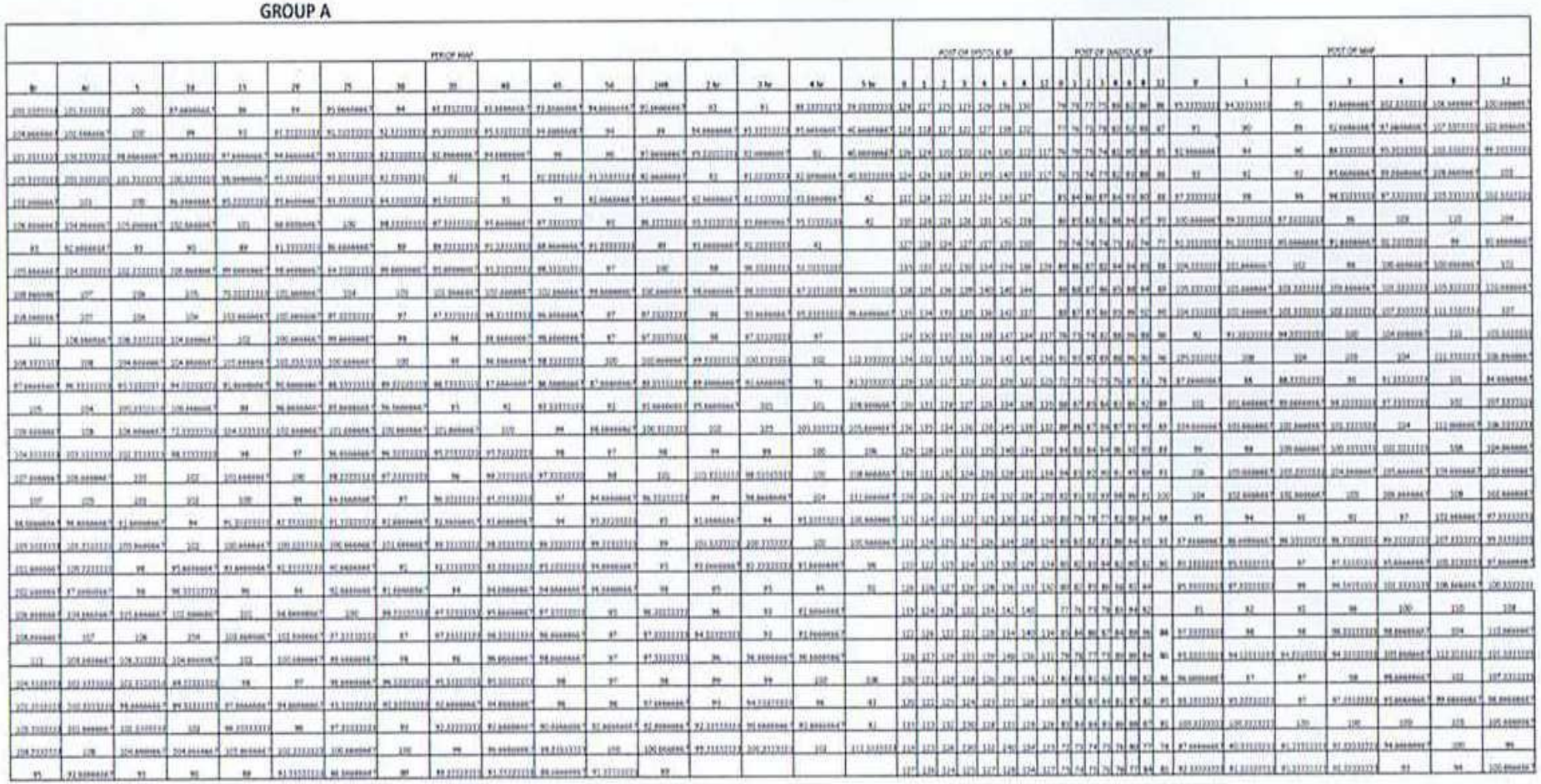
Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

GROUP A



GROUP A



GROUP A

VAS PAIN SCORE									
S.NO	0HR	2HR	4HR	6HR	8HR	12HR	16HR	20HR	24HR
1	0	0	2	4	2	2	1	1	0
2	0	0	2	4	0	0	1	2	2
3	0	0	3	0	0	1	2	2	1
4	0	0	2	3	0	1	1	2	2
5	0	0	4	0	0	2	2	1	1
6	0	0	1	3	0	0	1	2	2
7	0	0	4	0	0	1	1	1	1
8	0	0	3	3	0	0	1	2	2
9	0	0	4	0	0	1	1	1	1
10	0	0	3	4	0	0	2	2	2
11	0	0	1	3	0	0	1	1	1
12	0	0	2	4	0	0	1	1	1
13	0	0	2	4	0	0	1	2	2
14	0	0	3	4	0	1	1	1	1
15	0	0	1	4	0	1	1	1	1
16	0	0	2	4	0	0	1	1	1
17	0	0	4	0	1	1	2	3	0
18	0	0	3	4	0	0	2	2	2
19	0	0	2	4	0	0	1	1	1
20	0	0	2	4	0	0	1	1	2
21	0	0	2	4	0	0	1	1	3
22	0	0	3	4	0	0	2	2	2
23	0	0	4	0	0	1	1	1	1
24	0	0	2	2	4	0	1	1	1
25	0	0	2	3	4	0	2	2	2
26	0	0	2	4	0	0	1	1	1
27	0	0	3	4	0	0	2	2	2
28	0	1	3	4	0	1	1	1	1
29	0	0	2	4	0	0	1	1	2
30	0	0	4	0	0	1	1	2	2

GROUP B

S.NO	NAME	AGE	SEX	IP NO
1	DHARMENDRAN	43	M	36574
2	MUSTAFA	33	M	37778
3	SELVARAJ	48	M	24467
4	VASANTH	46	M	35678
5	JOSEPH	50	M	35789
6	PAZHANI	43	M	40234
7	RATHINAVEL	54	M	41233
8	SAROJA	49	F	38762
9	VEERAMAL	50	F	36743
10	MANOHARAN	55	M	37654
11	PAUL RAJ	45	M	36907
12	THANGAVEL	51	M	36542
13	RAMAMOORTHY	36	M	34567
14	NEELAMEGAM	58	M	37653
15	SARAVANAN	46	M	35876
16	SHANMUGAM	44	M	34213
17	MANGAYARKARASI	48	F	39821
18	RAISAIAH	62	M	40321
19	DEVENDRAN	55	M	38921
20	KANI	33	M	39472
21	VARADHRAJ	56	M	37482
22	LOGANATHAN	54	M	33674
23	VENKATESAN	66	M	34762
24	THANGARAJ	54	M	35681
25	GANESHAN	44	M	41234
26	SETHURAJ	48	M	36723
27	VELU	53	M	37642
28	VISHWANATHAN	48	M	38421
29	TAMIL SELVI	50	F	37621
30	NAGARAJ	33	M	36521

PERIOP HEART RATE

S.NO	BI	AI	5	10	15	20	25	30	35	40	45	50	1 hr	2 hr	3 hr	4 hr	5 hr
1	85	89	86	88	84	84	84	80	81	79	80	82	80	81	79	80	
2	104	102	115	100	99	96	94	93	92	91	90	96	94	93	94	92	93
3	105	104	102	100	99	98	97	94	96	92	91	90	87	89	88	88	
4	100	99	94	96	92	94	4	92	91	90	90	89	88	84	86	83	
5	94	89	92	90	91	90	89	88	87	86	83	85	84	82	81	80	84
6	88	92	90	81	89	88	84	86	88	81	80	79	78	80	84	82	88
7	94	90	91	89	88	87	86	84	82	81	80	84	83	82	80	84	86
8	86	87	76	75	83	82	84	85	86	81	80	79	78	76	75	76	78
9	81	80	79	76	78	75	78	76	77	75	74	70	71	73	74	75	76
10	92	90	87	88	85	84	82	81	82	83	84	82	80	88	87	85	87
11	90	87	85	86	89	84	83	81	80	79	78	76	75	79	80	78	79
12	98	94	95	92	90	89	88	88	87	86	85	90	91	88	86	85	89
13	104	102	100	103	103	100	101	98	97	93	92	91	90	84	97	96	95
14	100	98	92	93	94	95	87	92	91	90	93	94	92	91	90	94	85
15	98	96	94	93	92	90	93	94	92	91	90	88	86	84	82	81	89
16	96	95	92	93	90	89	88	88	87	85	84	83	82	79	80	84	85
17	94	92	93	91	90	93	90	91	89	88	86	85	87	87	88	85	84
18	96	88	87	86	85	89	79	78	76	77	75	78	79	77	82	83	84
19	94	92	90	91	87	88	83	84	87	84	83	82	80	79	83	84	
20	86	95	97	96	94	92	89	90	86	85	89	88	86	85	90	89	
21	76	77	78	79	76	79	80	83	76	75	74	73	72	70	67	68	66
22	83	84	86	87	86	88	84	83	82	80	81	78	79	78	77	76	77
23	88	87	85	84	83	80	81	79	78	76	75	74	78	77	76	80	82
24	87	86	85	84	83	82	80	78	76	75	4	73	76	75	78	80	82
25	86	85	83	80	78	76	75	74	74	76	75	77	75	78	82	81	80
26	81	81	79	78	76	75	74	73	72	77	78	76	73	71	71	71	70
27	85	84	83	82	81	80	79	77	73	74	73	72	71	70	71	76	74
28	90	89	84	86	83	82	80	79	77	76	74	73	76	71	76	78	82
29	86	84	83	82	89	78	77	74	73	72	70	71	70	72	74	72	74
30	87	84	83	84	84	85	82	81	80	79	76	75	74	83	72	70	76

POST OP HEARTRATE

S.NO	0	15	30	1HR	2HR	3HR	4HR	6hr	8HR	12 HR
1	78	76	78	76	79	76	76	77	75	89
2	90	89	88	90	91	94	92	96	104	100
3	90	91	94	96	94	92	94	96	118	94
4	87	86	82	81	80	83	85	80	100	85
5	82	81	80	84	85	81	89	90	94	90
6	86	81	81	84	83	84	90	90	95	88
7	81	82	83	84	86	88	89	90	86	94
8	80	81	85	84	83	82	84	85	89	90
9	77	74	71	74	71	76	73	88	84	84
10	89	89	87	90	91	90	90	91	96	87
11	83	84	85	86	87	88	88	88	93	96
12	92	93	94	95	90	91	92	94	102	98
13	94	92	91	89	84	87	92	94	98	104
14	96	95	96	93	94	92	85	96	101	97
15	86	85	84	85	90	91	90	92	98	94
16	85	84	87	88	86	85	87	88	96	93
17	83	87	81	87	86	88	89	90	95	89
18	82	81	80	77	84	88	89	90	95	90
19	84	82	83	80	81	84	82	85	94	87
20	88	88	87	90	92	90	92	95	100	93
21	68	69	70	68	71	73	72	76	84	73
22	78	79	80	81	82	80	81	83	98	82
23	80	81	80	82	81	83	83	85	90	84
24	82	80	82	81	85	83	84	85	94	83
25	79	80	82	93	83	82	84	86	93	84
26	74	75	73	78	78	76	76	80	84	80
27	74	75	77	75	79	81	83	87	90	84
28	83	82	82	83	84	85	84	88	93	86
29	79	76	75	74	78	82	83	89	88	83
30	71	76	77	78	75	81	83	90	88	89

PERIOP SYSTOLIC BP

S.NO	BI	AI	5	10	15	20	25	30	35	40	45	50	1 hr	2 hr	3 hr	4 hr	5 hr
1	134	131	132	130	128	127	126	124	122	120	119	118	125	124	124	128	127
2	128	129	130	123	124	125	129	122	120	117	122	128	124	125	120	121	120
3	131	130	128	127	124	122	120	119	119	119	120	118	118	127	24	126	124
4	136	134	132	130	129	128	124	122	120	119	118	117	118	120	122	124	122
5	138	134	136	130	128	126	122	123	124	126	124	125	126	127	128	126	94
6	126	123	120	121	119	118	17	120	121	122	124	126	122	121	120	119	126
7	128	124	122	121	20	124	122	124	121	124	120	122	121	120	124	125	127
8	137	136	133	132	134	135	130	129	127	128	122	125	124	125	126	130	133
9	138	136	135	132	130	129	128	126	127	125	126	127	122	120	119	124	135
10	136	132	130	129	129	128	124	125	122	120	119	118	120	122	124	126	127
11	129	128	125	124	120	119	118	117	118	120	121	129	134	125	134	123	122
12	144	141	140	139	137	136	135	133	130	134	132	131	130	129	127	129	134
13	138	133	134	135	132	129	127	126	129	130	132	134	136	131	132	130	132
14	127	121	124	122	119	115	117	125	126	120	118	117	118	116	120	122	121
15	135	131	130	129	127	126	123	120	119	117	118	124	131	119	120	121	123
16	138	135	134	133	132	130	129	128	126	25	125	121	120	119	117	118	120
17	136	135	132	131	129	128	126	125	124	126	129	129	127	126	128	130	133
18	142	140	134	135	134	132	130	128	127	128	126	123	120	118	112	128	138
19	135	134	130	131	129	127	120	118	119	117	118	117	129	129	125	127	90
20	136	133	132	134	130	128	126	127	128	129	126	125	122	120	128	127	
21	128	128	127	124	122	121	118	119	119	117	115	116	117	118	125	117	119
22	126	117	123	124	125	122	120	119	116	117	119	116	115	119	120	121	122
23	135	132	131	130	129	127	126	124	125	129	126	120	117	128	124	125	124
24	139	135	136	131	134	129	128	129	130	129	128	129	131	134	131	130	131
25	135	132	133	134	130	129	128	127	125	125	122	119	118	125	127	129	129
26	137	135	134	132	131	130	128	128	125	122	127	126	128	125	124	125	127
27	140	138	137	136	135	134	131	130	129	129	127	128	129	130	132	132	131
28	130	129	128	127	124	122	119	116	117	118	119	122	121	122	124	122	123
29	135	132	130	129	127	126	124	122	120	119	118	120	124	125	124	126	127
30	133	132	130	128	127	124	124	122	120	119	117	119	118	120	121	129	124

PERIOP DIASTOLIC BP

S.NO	BI	AI	5	10	15	20	25	30	35	40	45	50	1HR	2 hr	3 hr	4 hr	5 hr
1	89	85	84	83	80	79	78	75	76	77	78	79	80	81	84	82	81
2	76	74	72	71	74	72	71	70	73	74	72	71	70	73	77	70	72
3	82	84	87	86	80	82	80	79	79	77	79	81	84	89	88	89	86
4	88	87	86	84	83	82	81	80	79	7	74	76	80	81	82	83	84
5	80	91	89	88	86	85	83	81	80	79	76	77	76	74	83	88	
6	87	84	86	82	81	80	84	83	80	79	79	80	81	84	86	81	83
7	86	84	82	80	79	79	74	76	72	74	78	80	81	77	78	77	79
8	81	80	80	80	82	81	79	77	74	76	78	82	84	88	85	87	90
9	94	94	92	93	90	91	89	88	87	85	84	81	80	84	85	82	89
10	89	86	84	81	80	79	77	76	75	78	81	83	84	85	87	82	81
11	86	82	83	82	83	82	80	81	79	78	77	76	79	78	79	80	81
12	96	92	85	81	90	89	88	89	90	81	93	94	84	93	91	89	87
13	90	88	85	81	82	81	80	79	78	76	79	78	81	82	83	84	85
14	76	73	75	71	72	73	70	69	67	68	69	72	71	73	74	70	71
15	89	87	85	83	84	81	80	81	79	79	77	75	79	76	75	76	78
16	89	88	85	84	83	85	86	88	84	83	84	82	86	87	84	83	80
17	91	90	91	89	87	85	84	85	85	85	84	81	87	80	83	82	
18	90	91	90	86	85	83	80	81	78	76	78	79	80	82	88	90	89
19	80	83	84	81	80	79	76	75	77	79	78	80	74	75	77	76	78
20	80	87	86	85	84	83	82	80	79	76	75	74	78	79	76	83	
21	79	77	75	74	72	71	70	69	67	66	68	69	70	69	68	67	68
22	79	77	76	75	74	73	76	73	72	70	76	75	74	72	71	70	72
23	89	88	87	85	82	81	80	78	79	82	83	84	82	80	82	83	82
24	87	93	84	83	80	81	82	79		78	77	79	80	81	82	80	82
25	88	86	85	83	81	80	79	77	75	74	79	80	81	79	82	83	83
26	81	85	83	80	79	78	75	77	79	77	73	72	73	73	78	79	78
27	89	88	85	83	82	81	80	79	76	75	76	77	78	79	78	76	77
28	83	82	80	79	78	75	74	73	74	75	78	75	74	78	74	75	74
29	88	85	84	83	82	80	79	78	76	77	75	74	73	74	76	77	76
30	88	86	87	84	82	80	78	76	75	74	73	72	74	75	75	76	77

GROUP B

PEROP MAP																			POST OP SYSTOLIC BP								POSTOP DIASTOLIC BP								POST OP MAP							
0	1	5	10	15	20	25	30	35	40	45	50	55	1hr	2 hr	3 hr	4hr	5 hr	0	1HR	2HR	3HR	4HR	6HR	8HR	12HR	0	1HR	2HR	3HR	4HR	6HR	8HR	12 HR	0	1HR	2HR	3HR	4HR	6HR	8HR	12HR
104	102.3333333	101	98.66666667	96	95	94	91.33333333	91.33333333	91.33333333	91.66666667	92	94.33333333	95.33333333	97.33333333	97.33333333	103	106	105	104	103	101	104	109	106	105	89	88	87	84	83	85	89	94	101.3333333	100.3333333	98.33333333	96	95.66666667	98	101.3666667
93.33333333	93.33333333	98	98.33333333	97.66666667	89.66666667	88.33333333	87.33333333	88.66666667	90	88.66666667	88.33333333	88	90.33333333	88	87	98	72	74	73	74	75	75	78	75	88	90	90	91.33333333	91.66666667	87	95
98.33333333	99.33333333	100.6666667	99.66666667	94.66666667	95.33333333	93.33333333	92.33333333	91.33333333	91	91.66666667	93.66666667	95.33333333	100	98.66666667	100.6666667	98.66666667	80	79	78	79	79	80	84	86	96.33333333	95.33333333	94	94.33333333	95	99	100.6666667
104	102.6666667	101.3333333	99.33333333	98.33333333	97.33333333	95.33333333	94	92.66666667	94.33333333	93.66666667	93.66666667	92.33333333	94	95.33333333	96.66666667	96.66666667	84	82	80	81	84	86	90	92	97.33333333	96.66666667	96	98	100.3333333	102	108.3333333
106	105.3333333	104.6666667	102	100	98.66666667	95	91.33333333	94.66666667	94.66666667	93.33333333	93	92.66666667	91.66666667	94	99.33333333	101.3333333	79	78	76	74	84	88	92	94	94	90.66666667	93	92	100.3333333	103.3333333	108
100	98.66666667	97.33333333	95	93.66666667	91.66666667	91.66666667	94.66666667	92.66666667	93.33333333	93.33333333	95.33333333	94.66666667	96.33333333	97.33333333	93.66666667	95.33333333	125	124	120	121	122	124	130	124	84	82	85	80	84	85	90	89	97.66666667	96	94	93.66666667	96.66666667	98	105.3333333
100	97.33333333	95.33333333	91.66666667	94.33333333	91.33333333	89	92	88.66666667	90.66666667	93	94	94.66666667	91.33333333	93.33333333	93	89	127	124	128	121	122	130	124	130	80	85	78	79	83	89	80	88	95.66666667	95.33333333	93	93	99	102.6666667	94.66666667
105.6666667	104.6666667	103	97.33333333	98	99.66666667	96	94.33333333	91.66666667	92.66666667	92.66666667	95.66666667	97.33333333	97	99.66666667	105.3333333	104.3333333	110	111	111	110	114	116	112	117	88	85	84	85	80	89	92	87	102	100.6666667	99.66666667	99.66666667	104	104.6666667	108.6666667
110	108	106.3333333	106	101.3333333	101.6666667	102	100.6666667	100.3333333	98.33333333	98	96.33333333	94	96	97.66666667	96	104.3333333	114	113	111	110	109	114	110	117	88	84	85	87	90	92	98	90	103.3333333	100.3333333	100.6666667	101.3333333	103	106	112
104.6666667	101.3333333	99.33333333	97.66666667	98	94.66666667	92.66666667	91.66666667	90.66666667	92	93.66666667	94.66666667	96	97.33333333	99.33333333	96.66666667	96.33333333	133	132	130	129	134	134	140	134	87	83	81	85	84	85	90	88	99	99.33333333	97.33333333	98.33333333	100.6666667	101.3333333	106.6666667
100.3333333	99.33333333	97	96	95.33333333	94.33333333	92.66666667	93	92.33333333	92	91.66666667	94	95	94	94.33333333	94.66666667	94	124	125	128	124	123	126	131	130	84	82	83	81	84	90	88	97.33333333	96.33333333	97.33333333	95.33333333	94.33333333	98	104
112	108.3333333	108.6666667	107	105.6666667	104.6666667	103.6666667	103.6666667	103.3333333	106	106	106.3333333	106	105	103	102.3333333	103.6666667	132	131	130	134	132	149	145	135	88	86	87	89	88	94	100	96	102.6666667	103	105.3333333	104	106	112.3333333	115
104	101	101.3333333	102.3333333	98.66666667	97	95.66666667	94.66666667	95	94	96.66666667	96.66666667	95.33333333	98	99.33333333	99.33333333	99.33333333	134	137	137	132	129	133	134	140	86	85	84	82	81	84	87	94	102	100.6666667	99.66666667	98	97	100.3333333	102.6666667
95	93.66666667	91.33333333	89	87.66666667	87	85.66666667	87.66666667	86.66666667	85.33333333	85.33333333	87	86.66666667	87.33333333	89.33333333	87.33333333	87.66666667	122	121	121	120	124	128	129	129	79	72	73	74	75	76	79	80	91.33333333	89	89	89.33333333	91.33333333	93.66666667	94.33333333
104.3333333	101.6666667	100	98.33333333	98.33333333	96.66666667	94.33333333	94	92.33333333	91	90.66666667	93.66666667	91	95.66666667	90	91	93	127	128	128	130	132	134	140	136	77	75	79	82	83	84	91	89	93.66666667	92.66666667	94.66666667	98	99.33333333	100.6666667	108
105.3333333	103.6666667	101.3333333	100.3333333	99.33333333	100	100.3333333	100	98	95.66666667	97	95.33333333	97.33333333	97.66666667	95	94	99.33333333	129	124	127	128	134	136	142	134	84	81	83	81	80	85	92	88	97.66666667	96	97.66666667	98.66666667	98	102	108.6666667
108.6666667	105	104.3666667	103	101	99.33333333	98	97	98	98.66666667	99	97.33333333	96.33333333	95.33333333	98	94.33333333	153	134	133	135	134	136	138	153	85	84	85	88	89	89	94	89	99.66666667	100.6666667	101	103.6666667	104	104.6666667	108.6666667
108.3333333	107.3333333	104.6666667	102.3333333	101	99.33333333	98.66666667	98.66666667	94.33333333	95.33333333	94	95.66666667	93.33333333	94	96	101.6666667	105.3333333	138	137	136	134	132	134	136	140	86	85	84	89	90	88	92	89	103.3333333	101.3333333	101.3333333	100	97.33333333	103.3333333	108.6666667
104.3333333	100	99.33333333	97.66666667	96.33333333	94.33333333	92.66666667	89.33333333	91	91.66666667	91.33333333	92.33333333	89	91	93	93	92	126	128	129	130	129	133	139	133	79	80	83	80	84	85	90	91	94.66666667	96	98.33333333	100	99	101	106.3333333
104	102.3333333	101.3333333	101.3333333	99.33333333	98	96.66666667	95.33333333	95.33333333	93.66666667	92	91	92.66666667	92.66666667	93.33333333	97.66666667		128	129	130	134	132	133	139	130	84	82	83	83	84	86	92	86	98.66666667	97.66666667	97.33333333	100	100	101.6666667	107.6666667
94.66666667	93.33333333	92.66666667	90.66666667	88.66666667	87.66666667	86	85.66666667	84	88	83.66666667	84.66666667	85.66666667	85.33333333	85	83.66666667	85	120	121	123	123	125	126	130	124	69	70	71	71	74	76	83	74	88	87	88	89	91	97.66666667	95.66666667
94	93.66666667	91.66666667	90.33333333	91	89.33333333	90.66666667	88.33333333	87.33333333	89.66666667	90.33333333	89.66666667	87.66666667	87.66666667	87.33333333	88.66666667	88.66666667	123	122	123	124	126	125	127	125	74	73	74	75	72	74	83	73	90.33333333	89.33333333	90.33333333	91.33333333	90	90.33333333	97.66666667
103.6666667	102.6666667	101.6666667	100	97.66666667	96.33333333	95.33333333	93.33333333	93.66666667	96.33333333	97.33333333	98.66666667	97	95.33333333	96	97	96	120	124	124	129	130	133	136	132	83	84	86	84	85	87	92	89	97	98	98.66666667	99	100	102.3333333	106.6666667
104.3333333	102.3333333	101.3333333	99.66666667	98	97	97.33333333	95.66666667	95.66666667	93.33333333	95	94	95.66666667	97.33333333	98.66666667	96.66666667	98	133	131	130	134	137	137	141	134	82	83	81	80	84	85	90	82	99	99	98	98	101.6666667	103.3333333	107.3333333
108.6666667	107.3333333	105.6666667	103	99.33333333	97.33333333	96.33333333	94.66666667	93.66666667	91.33333333	90.33333333	91	93.33333333	94.33333333	94.33333333	94.33333333	94.33333333	128	127	128	132	129	134	135	134	79	77	80	81	83	84	89	83	98	99	99	100.6666667	101.3333333	103.6666667	106.6666667
98.66666667	97.66666667	96	95	92	90.66666667	89	87.33333333	88.33333333	89.33333333	90.33333333	90.66666667	89.66666667	91.33333333	91.66666667	91.66666667	91.66666667	123	124	126	125	127	128	134	128	79	77	78	79	81	84	88	80	91.66666667	91.33333333	94	94.33333333	96.33333333	98.33333333	105.3333333
103.6666667	100.6666667	99.33333333	98	95.33333333	94	92.66666667	90.66666667	91	89.33333333	89.33333333	90	91	93	93	93	93	124	122	123	129	133	135	139	132	77	79	82	84	86	86	91	88	91.66666667	91.33333333	95.66666667	99	101.6666667	105.6666667	107.6666667
103.6666667	101.3333333	100	98.66666667	97	94.66666667	93	91.33333333	90	88	87.66666667	87.66666667	88.33333333	90	90.33333333	91.66666667	92.33333333	124	126	127	128	130	131	136	128	78	76	77	79	85	86	94	88	93.33333333	92.66666667	93.66666667	95.33333333	100	101.3333333	108

GROUP B									
VAS PAIN SCORE									
S.NO	0HR	2hr	4hr	6hr	8hr	12hr	16hr	20hr	24hr
1	0	0	1	2	4	0	1	1	1
2	0	0	2	2	4	0	1	2	2
3	0	1	1	3	4	0	1	1	2
4	0	0	0	4	0	1	2	2	2
5	0	1	2	2	4	0	1	1	2
6	0	0	1	3	4	0	1	1	2
7	0	0	2	2	4	0	2	2	1
8	0	0	1	1	4	0	1	1	2
9	0	0	2	2	4	0	1	1	2
10	0	0	2	1	4	0	2	2	2
11	0	0	1	2	4	0	1	1	1
12	0	0	2	2	4	0	2	2	2
13	0	0	2	2	4	0	1	1	2
14	0	0	1	3	4	0	1	1	1
15	0	0	2	4	0	1	1	2	2
16	0	0	2	2	4	0	1	1	1
17	0	0	1	2	4	0	1	2	2
18	0	0	2	4	0	1	2	2	2
19	0	0	3	4	0	1	1	2	2
20	0	0	2	2	4	0	0	1	1
21	0	0	1	4	0	1	1	2	2
22	0	0	2	2	4	0	1	1	2
23	0	0	1	1	3	0	1	1	1
24	0	0	2	2	4	0	2	3	1
25	0	0	1	3	4	0	2	2	2
26	0	0	2	2	4	0	2	2	2
27	0	0	1	1	4	0	1	1	1
28	0	0	2	2	4	0	1	1	2
29	0	0	2	3	4	0	2	2	2
30	0	0	2	3	4	0	1	1	1